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BRITISH MEDICAL JOURNAL

LONDON SATURDAY DECEMBER 19 1953

STUDIES ON PANCREATITIS*

BY

ERIC G. SAINT, M.D., M.R.A.C.P.

AND

SARA WEIDEN, M.Sc.

(From the Clinical Research Unit of the Walter and Eliza Hall Institute of Medical Research and the Royal Melbourne Hospital)

In the same year as von Mering and Minkowski (1889) produced experimental diabetes in dogs by ligating the pancreatic duct, Fitz (1889), of Boston, described a case of "acute catastrophic inflammation of the pancreas." It is a regrettable fact that, 63 years later, the knowledge of exocrine and endocrine physiology of the gland, based on the brilliant work of Pavlov (1902), Bayliss and Starling (1902), and Banting and Best (1921–2), far outstrips the understanding of the clinical entities of pancreatitis. There are several reasons why this should be so: in the first place, pancreatitis is often difficult to diagnose, for the most suggestive symptom—pain—is variable both in site and in intensity, and is closely mimicked by other intra-abdominal conditions; secondly, diagnostic laboratory tests are by no means infallible; and, finally, little is known of the pathology of pancreatitis.

Acute and chronic pancreatitis have long been regarded as separate clinical and pathological entities, the one presenting as an acute abdominal emergency, and the other as a rare cause of abdominal pain, obstructive jaundice, wasting, steatorrhoea, or diabetes mellitus. Comfort *et al.* (1946) have established a link between acute and chronic pancreatitis in their now classical description of "chronic relapsing pancreatitis." Not the least important part of their work was to draw attention to the aetiological significance of alcoholism.

The publication of several reviews on acute pancreatitis (Paxton and Payne, 1948; Warren, 1948; Lipp and Aaron, 1950; Roberts *et al.*, 1950), on subacute pancreatitis (Gray *et al.*, 1938; Macnab, 1949), and on chronic relapsing pancreatitis (Maimon *et al.*, 1948; King, 1949; Gambill, 1949) indicates the amount of contemporary interest in the subject. In Australia, Rose (1951) and Heinz (1952) have reviewed experience in Sydney and Melbourne. While these statistical surveys provide an important overall picture of the incidence and complications of pancreatitis, they are less helpful with regard to information on pathogenesis and individual clinical patterns.

The present work was undertaken, (1) to investigate the clinical features of acute and chronic pancreatitis; (2) to elucidate some of the aetiological factors involved; (3) to study possible associated disturbances in gastric and hepatic function; (4) to evaluate laboratory tests as aids to diagnosis; and (5) to clarify the position with respect to treatment.

Between October, 1951, and July, 1952, 24 cases of acute and chronic pancreatitis were studied.

Methods of Study

In addition to full clinical examination, diet histories were taken by Miss C. N. Turner (dietitian at the Clinical Research Unit of the Walter and Eliza Hall Institute of Medical Research and Royal Melbourne Hospital). The following investigations were also made:

(1) *Estimation of urinary diastase*, using Dodds's modification of Wohlgemuth's method (Dodds and Dickens, 1925), was carried out during attacks of pain.

(2) *Intravenous Secretin Test.*—The method of Dornberger *et al.* (1948), based on the original studies of Agren *et al.* (1936), was closely followed. A double lumen tube was swallowed by the patient in the fasting state. The progress of the tip of the tube into the duodenum was followed fluoroscopically. Gastric contents were aspirated by Wangensteen suction and the duodenal contents were collected in 30-ml. test-tubes under slight negative pressure (estimated at 20 mm. Hg). After two ten-minute samples of fasting duodenal content had been aspirated, Wyeth's secretin was given intravenously, in a dosage of 1 unit per kg. body weight. The total volume and the bicarbonate content of each sample, estimated by the titrimetric method of Van Slyke, were recorded.

(3) *Gastric Function.*—A histamine test meal was done on most patients, many of whom also had gastric biopsy performed.

(4) *Liver Function.*—Estimation of serum bilirubin, alkaline phosphatase, serum proteins, and the cephalin-flocculation test was performed on most patients. A few also had a liver biopsy done.

(5) *Oral Sugar Tolerance Test.*

(6) *Gelatin Absorption Test.*—This test of protein digestion, based on a technique described by Krauel (1944), was performed on four patients. Gelatin, 50 g., was given orally, and the level of the serum amino-nitrogen was followed at hourly intervals for five hours.

(7) *Radiological Studies.*—Plain *x*-ray films of the pancreatic area and barium meal *x*-ray films were taken in most patients, and where cholecystectomy had not previously been performed a cholecystogram was done.

*An abbreviation of this paper was presented to the Australasian Medical Congress (British Medical Association) in August, 1952. The work was aided by a grant from the National Health and Medical Research Council, Australia.

Acute Pancreatitis

Eleven cases of acute pancreatitis were studied. The age and sex incidence of patients is shown in Fig. 1. In 10 of these cases the diagnosis was made either on clinical grounds or at laparotomy, but in one case severe pancreatitis was an unsuspected and surprising finding at necropsy. Two of these patients died.

Pain and persistent vomiting were the most frequently presenting symptoms. The pain was felt in the epigastrium and radiated to the right and left hypochrondrium, and through to the back at the level of the twelfth dorsal to the second lumbar vertebrae. The quality and intensity of the pain were rarely, however, of great diagnostic value: in two patients right-sided localization closely simulated biliary colic, and in two other patients the wide area of reference suggested the diagnosis of a perforated peptic ulcer. An initial error in diagnosis was made in no fewer than five cases out of the eleven under review.

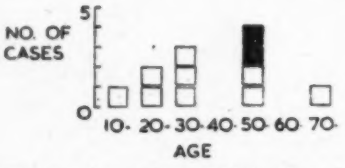

FIG. 1.—Age and sex distribution of 11 cases of acute pancreatitis. White squares, males; black squares, females.

The duration of the pain and the degree of abdominal tenderness and rigidity were very variable. A useful diagnostic physical sign was observed in one patient: that first described by Grey Turner—a cyanotic discoloration of the skin of the left loin and in the peri-umbilical area.

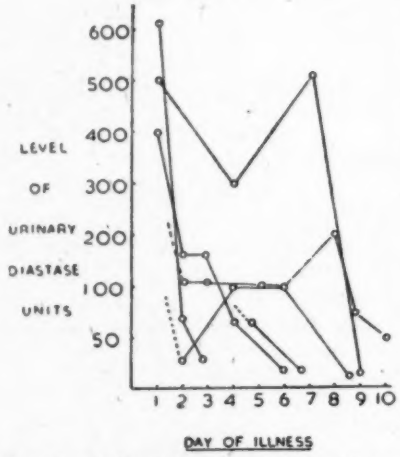

FIG. 2.—Serial urinary diastase levels in six cases of acute pancreatitis.

In five patients jaundice of mild degree (serum bilirubin 3–6 units per 100 ml.) was present within a few hours after the onset of abdominal pain. Biochemical tests showed this to be of obstructive type. Transient glycosuria was noted in two cases within 48 hours of onset, and in one fatal case acute diabetic coma developed five days after the onset of symptoms.

Estimation of the urinary diastase was of great help in the differential diagnosis of pancreatitis from other acute abdominal conditions. A level of over 100 units is diagnostic of pancreatitis. Although moderate elevation of the urinary diastase has been observed in some cases of perforated peptic ulcer, the significantly high levels, 400–1,000 units, which at times are found in patients with acute pancreatic necrosis should guide the surgeon in this often difficult clinical problem. Serial diastase levels in six cases are shown in Fig. 2. It will be seen that there is a tendency for the diastase to fall to normal levels within two to five days after the onset of pain. Estimation of the urinary diastase test is therefore of real value only if it is done soon after the onset of pain.

Aetiology

Cases fell into three aetiological groups: (1) associated with gall-stones; (2) associated with alcoholism; and (3) apparently due to primary infection.

(1) *Cholelithiasis* (three cases).—Halsted (1901) and Opie (1901) were the first to point out the association of pancreatitis with a calculus obstructing the ampulla of Vater. In most reviews on acute pancreatitis, gall-stones have been present in 50–80% of patients. In the present limited series of cases the relatively few patients with proved gall-stones is quite a striking feature.

In one patient it was possible to obtain useful correlation between the clinical features and the histological findings in both the liver and the pancreas.

A 73-year-old man with hypertensive vascular disease developed acute abdominal pain and vomiting, and became slightly jaundiced. Laparotomy was performed. The head of the pancreas was swollen and indurated. Material was obtained from this site with a liver biopsy needle; and liver tissue was also taken for section. Cholecystenterostomy was performed. The pancreas showed acute inflammatory changes (Fig. 3), and in the liver severe cholangitis was present.

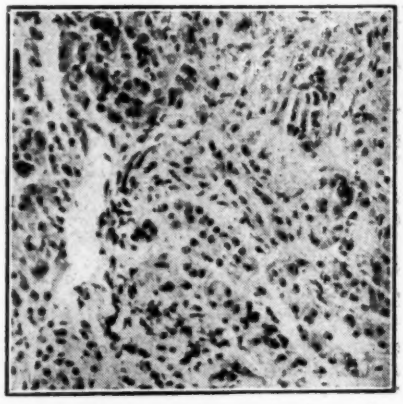

FIG. 3.—Section of pancreatic tissue obtained by means of an aspiration liver biopsy needle at laparotomy in a man with pancreatitis complicating cholelithiasis, showing acute interstitial inflammatory changes. (Haematoxylin and eosin. ×150.)

Two factors are involved in the production of pancreatitis when calculi obstruct the ampulla: the mechanical reflux of bile into the pancreatic duct causes an acute chemically induced inflammatory reaction; and, as in this patient with obvious cholangitis, bacterial infection undoubtedly plays an important part.

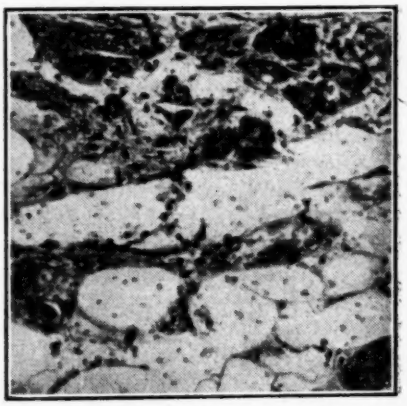

FIG. 4.—Section of pancreas showing acute necrosis in a woman dying of acute infectious hepatitis.

(2) *Alcoholism* (five cases).—Many early writers—for example, Egdahl (1907)—noted that acute pancreatitis often followed a bout of heavy drinking. Five of the patients under review were exceptionally heavy beer or spirit drinkers, but in none of them was there any evidence of biliary disease. It is of possible significance that all of them had arterial hypertension. In three patients pain followed a bout of heavy drinking.

In February, 1952, a 32-year-old man had severe abdominal pain after a drinking bout. His urinary diastase was 400 units. Five days after admission he lapsed into diabetic coma. He improved with insulin but died two days later from bilateral bronchopneumonia. At necropsy severe pancreatic necrosis was found. The common bile duct and gall-bladder were normal. It is of great interest that an identical twin brother of this patient also had severe pancreatic necrosis, from which he recovered, in 1949.

Two patients had recurring attacks of abdominal pain related to alcoholic episodes. That pancreatitis of this nature is primarily a medical rather than a surgical problem is indicated by the fact that recurrence of pain in these two patients ceased in a period of nine months' observation when they stopped drinking and were able to eat good diets.

(3) *Infection* (two cases).—Certain viruses are known to cause acute pancreatic inflammation. Mumps is the classical example, of which there was one instance in this series. Poppel and Bercow (1949) noted symptoms referable to pancreatitis in no fewer than 17 of a series of 95 cases of mumps. Since both mumps orchitis and meningoencephalitis without parotitis are known to occur, it is conceivable that occasional obscure cases of pancreatitis may be due to infection with the mumps virus, without demonstrable enlargement of the parotid glands.

Pancreatitis is occasionally an associated condition in severe cases of infectious hepatitis (Lucké, 1944).

A middle-aged woman developed classical signs and symptoms of infectious hepatitis and died in hepatic coma. At necropsy widespread necrosis of the liver cells was found, and the pancreas showed necrotic changes (Fig. 4).

Transient elevation of the urinary diastase has been noted in several cases of acute infectious hepatitis of moderate severity; it is possible that mild pancreatitis may be a common complication of infectious hepatitis.

A strain of Coxsackie virus pathogenic to man is known to cause acute pancreatitis in suckling mice (Pappenheimer *et al.*, 1951), but so far pancreatitis attributable to this virus has not been recognized clinically.

Treatment

The diagnosis of acute pancreatitis may present considerable difficulty, and if an occasional laparotomy is needlessly performed little harm to the patient is likely to follow. Nevertheless, if the diagnosis of acute pancreatitis can be assured conservative treatment is urged.

Pain was satisfactorily controlled with pethidine. Morphine may actually aggravate pancreatic pain.

Continuous *gastric aspiration* was applied until pain and vomiting ceased. Aspiration of gastric juice prevents vomiting and inhibits the hormonal stimulation of the flow of pancreatic juice.

Loss of electrolytes necessitated accurate replacement with intravenous glucose-saline and potassium chloride. Edmondson *et al.* (1952) and Roberts *et al.* (1950) have drawn attention to the dangerous degree of hypochloraemia and hypokalaemia which may occur in pancreatic necrosis; and a factor which the former authors show to have been hitherto neglected is the binding of calcium when fat necrosis is extensive, indicating that intravenous injections of calcium gluconate should be given in severe cases.

Although acute diabetes is a rare complication, the urine and blood sugar should be repeatedly estimated and insulin given when necessary.

Secondary infection is a threat to life in acute pancreatic necrosis. Therefore penicillin (500,000 units six-hourly) and streptomycin (0.5 g. twice daily) were given to all cases.

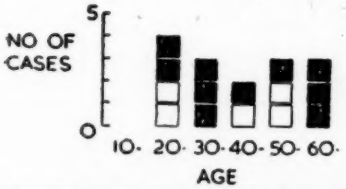

FIG. 5.—Age and sex distribution of 15 cases of chronic pancreatitis. White squares, males; black squares, females.

In cases in which clinical or radiological evidence pointed to cholelithiasis elective cholecystectomy was performed *after the attack of pancreatitis had subsided.*

Chronic Pancreatitis

Chronic pancreatitis is in some respects a misnomer, for the natural history of the majority of the 15 patients studied (see Fig. 5) pointed to a relapsing, recrudescent form of disease. The pathology which was observed in patients on whom operation was performed during attacks of pain was that of oedema or haemorrhagic necrosis of the gland. In several patients these repeated attacks had ultimately caused destruction of the acinar and islet tissue, with fibrosis and even calcification, leading to deficiency of both internal and external secretion.

The clinical history of four male patients closely resembled the description of chronic relapsing pancreatitis given by Comfort *et al.* (1946). Another syndrome was that observed in eight female patients who had attacks of pancreatitis following cholecystectomy. The remaining three patients formed a miscellaneous group.

Chronic Relapsing Pancreatitis

All four patients were males. Three of them had essential hypertension; three had been heavy consumers of alcohol. Three patients had a laparotomy performed at one time or another, and, although pancreatitis was noted, there was no evidence of associated biliary disease.

The initial manifestation of the disease was that of recurring attacks of abdominal pain, during which the urinary diastase was raised. In one patient only a few weeks intervened between attacks of pain, but in the remainder several months of freedom from pain were enjoyed. Sometimes a distressing feature was that pain persisted despite a variety of operations undertaken on the biliary tract.

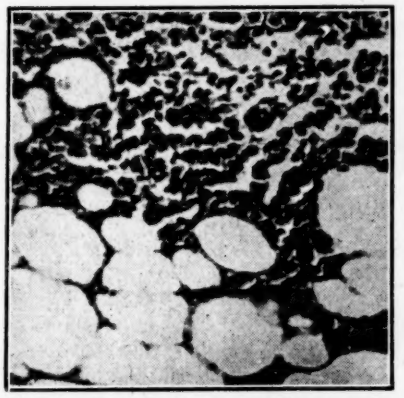

FIG. 6.—Section of pancreas from a case of chronic relapsing pancreatitis. The gland was considerably shrunken. Much of the acinar tissue has been replaced by fat. (Haematoxylin and eosin. ×150.)

A 51-year-old man, once a heavy beer-drinker, had been admitted to hospital on 16 occasions between 1944 and 1951 with attacks of pancreatic pain. In 1944 his gall-bladder had been removed, but when examined it did not appear to be diseased. Twice the common bile duct was drained during attacks of pain. Ultimately he became a pethidine addict. In one attack of pain relief was obtained by bilateral splanchnic block; a right-sided sympathectomy, removing ganglia from D 8 to L 2, seemed to give more prolonged relief until his death two months later from spontaneous intraperitoneal haemorrhage. Investigations showed impaired fat absorption, a mild diabetic type of sugar-tolerance curve, achlorhydria, and atrophic gastritis. At necropsy the pancreas was shrunken, and histologically showed replacement of much of the pancreatic acinar tissue by fat (Fig. 6). Severe atheroma of the aorta was present.

The disease tends to be progressive, and in less fortunate patients the replacement of acini by fibrotic tissue and deposits of calcium may have profound metabolic effects.

A 49-year-old man had frequent attacks of pancreatic pain and ultimately developed diabetes mellitus. Pain made life

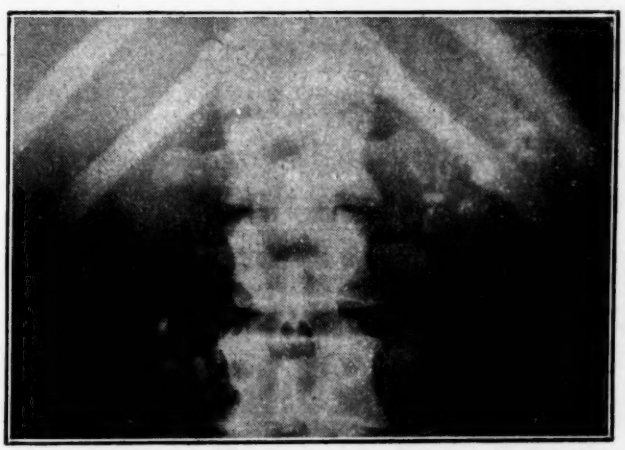

FIG. 7.—*X*-ray film of the pancreatic area in a middle-aged man with relapsing pancreatitis and diabetes mellitus, showing diffuse calcification throughout the gland.

intolerable, and he lost 3 st. (19 kg.) in weight. Investigations showed impaired fat absorption and poor gelatin digestion. An x-ray film of the pancreatic area (Fig. 7) showed diffuse calcification.

The diagnosis of chronic relapsing pancreatitis is based on the history of recurring episodes of upper abdominal pain without other obvious cause, and evidence of deficiency of either internal or external pancreatic secretion, such as glycosuria and hyperglycaemic sugar tolerance (see Fig. 8), frank steatorrhoea, wasting, or a low flat type of gelatin absorption (see Fig. 9). The finding of a raised urinary diastase is of the utmost importance in diagnosis in obscure cases. In advanced cases a search should be made radiologically for pancreatic calcification.

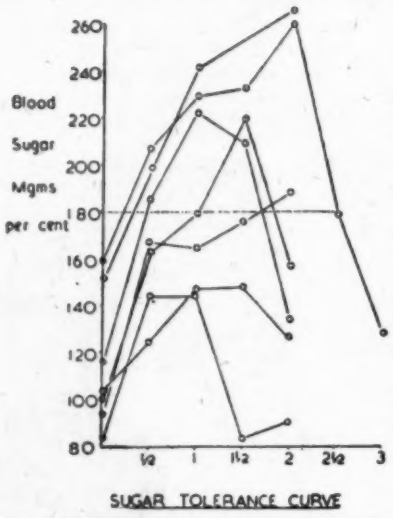

FIG. 8.—Oral sugar tolerance curves in seven cases of chronic pancreatitis.

In three cases liver biopsy was performed. In one case mild fatty change, presumably of nutritional origin, was found. Gross degrees of fatty change and actual cirrhosis have been noted by other observers (for example, Fiessiger and Olivier, 1933; Snell and Comfort, 1937; Sharp *et al.*, 1952). Whether these cirrhotic changes in the liver develop *pari passu* with pancreatic fibrosis as a result of suboptimal nutrition, or whether they are the result of impaired digestion of fat and protein due to pancreatic insufficiency, is open to debate. In one case gastric biopsy showed severe atrophic gastritis.

The *treatment* of chronic relapsing pancreatitis is a problem beset with extraordinary difficulties. In the early stages recurrent attacks of pain may be prevented by improving the diet and enforcing strict abstinence from alcohol; but with regard to the more advanced cases there is at present no uniformity of opinion regarding the correct course of action which should be taken. Many American surgeons advise interruption of the afferent nervous pathways, either by limited splanchnic nerve section (de Takats, Walter, and Lasner, 1950) or unilateral sympathectomy (Hurwitz and Gurwitz, 1950), or by the more radical bilateral lumbo-dorsal sympathectomy combined with splanchnicectomy (Connolly and Richards, 1950). However, Cattel and Warren (1952) maintain that these measures offer only temporary relief from pain and advise pancreatico-duodenectomy.

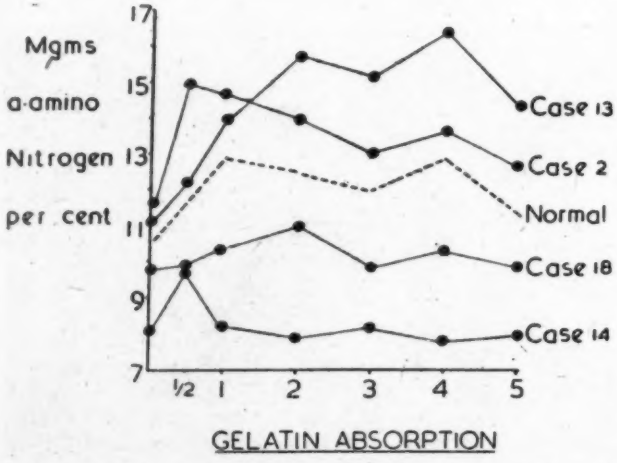

FIG. 9.—Gelatin absorption curve in four cases of chronic pancreatitis. The level of amino-nitrogen is followed at intervals for five hours after the administration of gelatin (50 g.).

Our own experience is too limited to be of value. In three patients the pain was temporarily abolished by bilateral splanchnic block. In only one patient was a limited sympathectomy performed, and his early death two months after operation prevented adequate assessment of the result.

Relapsing Pancreatitis Following Cholecystectomy

All eight female patients in this group had what might be called the "gall-stone diathesis"—most were obese, most had hypertension, and three were known to have had diabetes mellitus for some time. In all patients calculi were present when the gall-bladder had been removed. Often within a few months of cholecystectomy these patients experienced attacks of upper abdominal pain. Often this was felt below the right costal margin, and led them to believe that their preoperative biliary colic had returned. Abnormally high levels of urinary diastase were noted during these attacks.

An obese 45-year-old woman with mild diabetes mellitus had her gall-bladder removed for cholelithiasis. Six months later she had a severe attack of abdominal pain lasting two days. The urinary diastase was 1,000 units. Two further attacks occurred and on each occasion the diastase was raised.

In some cases it was noted that pain followed an unusually large fatty meal. Alcoholism and frank dietary deficiency did not seem to be causative factors; in fact, improvement in many cases occurred when measures were taken to reduce weight by advising smaller non-fatty meals.

It seems likely that many patients suffering from the so-called "post-cholecystectomy syndrome" have, in fact, a mild recrudescent pancreatitis. Doubilet and Mulholland (1949) maintain that spasm of the sphincter of Oddi may cause a rise in pressure in the common bile duct sufficient to lead to regurgitation of bile into the pancreatic duct in patients with a common channel. It is known that bile injected experimentally into the pancreatic duct causes chemical inflammation. They advise section of the sphincter; but we regard the factual basis of their hypothesis as unproved, and none of our patients have been subjected to this operation.

Other Causes of Chronic Pancreatitis

A 23-year-old woman with a long history of ulcerative colitis and a grossly deficient diet had an attack of severe abdominal pain. At laparotomy acute pancreatitis was found, but the organ was also fibrous, indicating chronic pathological change.

Ball *et al.* (1950) described interstitial chronic inflammatory changes in a high proportion of cases of ulcerative colitis examined at necropsy. Since nutritional hepatitis is also common in ulcerative colitis it is reasonable to assume that malnutrition plays an important part in the causation of pancreatitis in this condition.

A 34-year-old woman had infectious hepatitis in 1949. This was followed by frequent attacks of abdominal pain. All investigations were negative except for the finding of high diastase levels up to 152 units during the attacks.

The clinical evidence was in favour of a direct causative relationship between this patient's pancreatitis and the original infection with the virus of infectious hepatitis.

A 26-year-old man had attacks of upper abdominal pain and intermittent jaundice of obstructive type. He also had symptoms of diabetes mellitus. At laparotomy the pancreas was fibrotic and indurated, but the gall-bladder and common duct were normal. The gall-bladder and common duct were drained and the jaundice subsided.

No obvious cause of chronic pancreatitis was found in this case. Obstructive jaundice is not an uncommon manifestation of chronic pancreatitis (Selesnick, 1952), and this case illustrates an important point in the surgical management.

When the gall-bladder is not diseased, under no circumstances should it be removed, for later it may be used with advantage in a short-circuiting operation for the relief of jaundice.

Intravenous Secretin Test

The results of this test in eight normal subjects, five patients recovering from acute pancreatitis, and eleven patients with chronic pancreatitis are shown in Fig. 10. In each group a very wide range of values of both volume and bicarbonate content of the duodenal contents was found.

Although there is an obvious statistical tendency towards lower volumes and bicarbonate content in patients recovering from acute pancreatitis and in patients with chronic pancreatitis, the degree of overlap in values as compared with normal healthy subjects is enough to render the test unsuitable for ordinary diagnostic purposes. Dornberger and his colleagues arrived at a similar conclusion. It would seem that only when parenchymal damage is very severe and extensive is one likely to obtain significantly low values with this test, which also has the disadvantage of being both expensive and time-consuming.

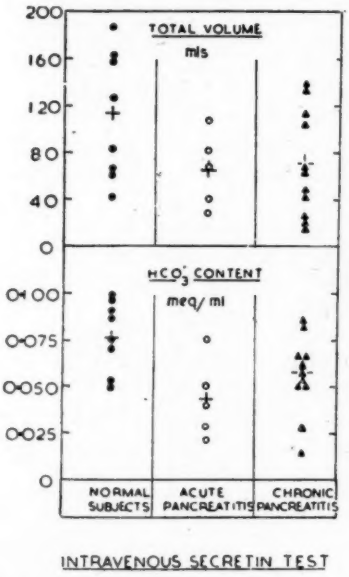

FIG. 10.—Scatter diagram showing volume and bicarbonate content of duodenal aspirate after the administration of secretin intravenously to eight normal subjects, five patients recuperating from acute pancreatitis, and eleven patients with chronic pancreatitis. + = mean value.

Discussion

With respect to pancreatitis it is clear that there are many unsolved problems. Even clinical recognition is not always an easy matter: acute pancreatitis is not always correctly diagnosed, and chronic pancreatitis may manifest itself under a number of guises which may tax the diagnostic skill of the clinician. Once an increased awareness of this condition becomes prevalent among physicians and surgeons, however, and once the habit of calling for urinary diastase estimations in cases of obscure abdominal pain is acquired, it is likely that more cases will come to light, with opportunities for further study.

One of the difficulties encountered in the diagnosis of milder cases of acute and relapsing pancreatitis is the lack of reliable laboratory tests. The finding of high levels of pancreatic enzymes, either in the serum or in the urine, should suggest pancreatitis, but there is evidence that such elevation is often transient. In our hands the secretin test has been of little practical value. Innerfield *et al.* (1952a, 1952b) have demonstrated a high level of plasma antithrombin activity in both acute and relapsing pancreatitis, and it is possible that this may prove to be a subtle laboratory test of considerable value. In suspected chronic pancreatitis, steatorrhoea (faecal fat content more than 30%), a hyperglycaemic sugar-tolerance curve, and calcification of the pancreas should be looked for.

If these investigations prove negative despite a strong clinical suspicion of pancreatitis, diagnostic laparotomy is justifiable. The pancreas should be carefully inspected and palpated. However, it is believed that closer correlation between naked-eye appearances and actual histology is demanded, and to this end a technique of obtaining biopsy material is being developed, using a Franseen aspiration liver biopsy needle (the material shown in Fig. 3 was obtained by this means).

In the attempt to elucidate the aetiology of pancreatitis it was apparent that a heterogeneous group of conditions was being grouped under one heading only by virtue of the fact that one organ, the pancreas, was predominantly affected. Now the only things shared in common by infectious hepatitis, Laennec's cirrhosis, infectious cholangitis, and xanthomatous biliary cirrhosis are pathological changes in the liver resulting in jaundice, yet we do not refer to these diseases collectively as "hepatitis." The same reasoning may with justification apply to the pancreas. Chronic pancreatitis complicating ulcerative colitis is a totally different entity from pancreatitis following cholecystectomy; likewise, pancreatitis complicating biliary calculi has an entirely different pathogenesis from that occurring in alcoholic subjects.

What are the factors known and believed to be the cause of pancreatitis? Trauma to the pancreatic ducts, during gastrectomy for example (Millbourn, 1949), causes pancreatic inflammation. Any condition which causes reflux of bile into the pancreatic ducts may also produce pancreatitis. This is presumably the mechanism in those cases of pancreatitis following cholecystectomy in which pressure gradients in the common bile duct are believed to be disturbed. When calculi obstruct the ampulla, in addition to reflux along the "common path," infection is probably an added factor.

There is accumulating clinical and experimental evidence that, as with the liver, certain foodstuffs have a protective action on the pancreas. Fatty changes and fibrosis in the pancreas have been shown to be present (Waterlow, 1948; Davies, 1948) in undernourished native races at necropsy. Necrotic pancreatic lesions have been demonstrated in rats fed on a low-protein diet (Lindsay *et al.*, 1948). It is probable that methionine is an essential protective metabolite, for when the ethyl analogue of methionine, ethionine, which blocks the utilization of methionine, is fed to experimental animals pancreatic necrosis invariably occurs (de Almeida and Grossman, 1952). The clinical counterpart of these experimental findings is the type of pancreatitis which occurs in malnourished alcoholic patients and as a complication in patients suffering from ulcerative colitis. In alcoholic patients there is also the possible additional aetiological factor of the stimulation of excessive quantities of pancreatic juice during a drinking bout. In our studies with the double lumen tube it was noted in control subjects that the rate of flow of duodenal aspirate was trebled when 2 oz. (57 ml.) of brandy was introduced into the stomach.

The presence of arterial hypertension in a high proportion of patients with pancreatitis has been commented upon by Heinz (1952). Care must be taken in interpreting these statistics, for many patients of middle age with cholelithiasis, who comprised a large number of his cases, tend to have the obese hypertensive diathesis. There are a few hints, however, that this correlation may not be entirely coincidental, for there are on record in the literature a number of cases of pancreatitis complicating familial hypercholesterolaemia (Holt *et al.*, 1939; Collett and Kennedy, 1948; Klatskin and Gordon, 1952). There is evidence also that genetic factors may be involved in the causation of chronic relapsing pancreatitis. Comfort and Steinberg (1952) reported on a family in which the condition occurred in four generations; our own observation of acute pancreatic necrosis occurring in identical twins is also of interest. The relationship between hypercholesterolaemia and the development of atherosclerosis is well known, and it is an intriguing possibility that vascular disease may be at least a condition which predisposes to the development of pancreatitis.

Finally, the possibility of a virus infection, either of mumps or of infectious hepatitis, must not be disregarded in obscure cases.

Thus a variety of aetiological factors, acting either alone or in combination, may lead to pathological change in the

pancreas sufficient to cause clinical manifestations. The following entities can be quite sharply differentiated: (1) *Traumatic pancreatitis*, following surgery of the stomach and duodenum; (2) *virus pancreatitis*, complicating mumps and possibly infectious hepatitis; (3) *reflux pancreatitis*, complicating biliary calculi and following cholecystectomy; (4) *chronic nutritional pancreatitis*, or "chronic relapsing pancreatitis," occurring in malnourished alcoholic patients; (5) *metabolic pancreatitis*, complicating hyperlipaemia and hypercholesterolaemia.

The difficult problem of treatment must be approached with this aetiological perspective in view. Surgery plays no part in the immediate management of acute pancreatitis, when electrolyte replacement and the prevention of secondary infection are considerations of life-saving importance. When acute symptoms have subsided an attempt must be made to assess the predominant aetiological factor involved; if radiological studies reveal the presence of biliary calculi cholecystectomy should be performed, but if there is no evidence of gall-bladder disease cholecystectomy is absolutely contraindicated, for it may be necessary to use the gall-bladder later in a short-circuiting operation if further attacks of pancreatitis lead to obstructive jaundice. If the patient is an alcoholic, abstinence must be enforced and a high-protein diet advised. All that can be said at the present time about reflux pancreatitis following cholecystectomy is that control of weight and limitation of fat intake have yielded good results: one waits for further reports from those surgeons who courageously perform ampullary sphincterotomy.

The position with regard to surgery in chronic relapsing (nutritional or metabolic) pancreatitis is still by no means settled. If it is proved that splanchnicectomy and lumbodorsal sympathectomy offer only temporary relief from pain it will be necessary to resort to pancreatico-duodenectomy. This might seem an unwarranted surgical risk, but such is the severity of the pain and the misery of the patient that heroic measures are called for in some cases. Moreover, in competent surgical hands these risks have been greatly reduced, as has been shown by Smith and Brown (1952), in their experience of surgery of carcinoma of the pancreas.

Summary

The clinical features and laboratory investigations in 24 proved cases of acute and chronic pancreatitis have been studied at the Royal Melbourne Hospital, Melbourne, Australia.

It is felt that the confusion of thought which exists on this subject might in part be dispelled if attention was paid to aetiological aspects of the problem. Reasons are presented for considering traumatic pancreatitis, virus pancreatitis (mumps and infectious hepatitis), "reflux" pancreatitis, chronic nutritional pancreatitis, and metabolic pancreatitis as distinct clinical entities.

In acute pancreatic necrosis good results were obtained with conservative treatment—continuous aspiration of the gastric contents, electrolyte replacement, and the administration of antibiotics.

Chronic relapsing (nutritional) pancreatitis is a condition characterized by recurrent attacks of pancreatic oedema and necrosis causing pain; ultimately destruction of the gland and replacement fibrosis lead to wasting, steatorrhoea, and diabetes. Pancreatic calcification is occasionally visible radiologically and induration of the head of the pancreas may cause obstructive jaundice.

In the absence of biliary calculi, cholecystectomy is contraindicated in chronic pancreatitis. When severe and unremittent pain becomes a feature in advanced cases a choice must be made between sympathectomy and pancreatico-duodenectomy.

Relapsing "reflux" pancreatitis was found to occur in female patients following cholecystectomy. Further data on the mechanics of the sphincter of Oddi and the common bile duct are required before agreement on the surgical relief of these patients can be reached.

The diagnosis of mild cases of acute and chronic pancreatitis may be difficult. Although elevation of the urinary diastase level is helpful this may be only transient. Collateral evidence of steatorrhoea, glycosuria, pancreatic calcification, and impaired protein digestion should be sought for in diagnosing chronic pancreatitis of all types.

We wish to thank those members of the honorary medical staff of the Royal Melbourne Hospital who kindly referred patients for investigation. We also wish to acknowledge the help we have received from our colleagues in the Clinical Research Unit.

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In an appeal for funds, signed by Dr. Elliott P. Joslin, the president, the Diabetes Foundation announces that it was incorporated in 1953 with wide powers to include not only activities concerning the support of research and camps for diabetic children, formerly dealt with by separate funds, but also the administration of a new hospital teaching clinic which it is hoped to build as soon as the necessary money is available.

L-NORADRENALINE IN TREATMENT OF SHOCK IN CARDIAC INFARCTION

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Cardiac infarction is more often than not accompanied by shock. Usually it is transient and passes off as the pain abates under the influence of morphine. In some patients it persists and appears to contribute to an early fatal issue, while, in a few, shock gravely complicates the clinical state during a period of several days or even a week in an illness which in four cases out of five ends in death. It is in this last group that physicians have felt the lack of therapy to combat peripheral circulatory collapse, in which pressure may fall to levels that can hardly, if at all, be recorded, with disappearance of pulse and loss or clouding of consciousness. Intravenous infusions of hypertonic glucose, plasma, blood, and dextran have been used, and slight success has been claimed. In spite of its obvious possibilities, adrenaline has been discarded in this condition; it may raise the pressure but the risk of ventricular fibrillation is too great. On the other hand, other pressor drugs of the sympathomimetic amine series have been shown to raise the blood pressure without increasing the rate or the work of the heart. It was the claim of anaesthetists that the laevorotatory form of noradrenaline secured their patients against serious falls of pressure during major operations which led us to the use of this substance in cardiogenic shock. In this paper we report the results of the use of L-noradrenaline bitartrate ("levophed") in the six instances in which we have employed it for this purpose.

Material and Methods

We have, so far, treated only six patients suffering from shock in myocardial infarction with infusions of L-noradrenaline bitartrate, restricting this treatment to those patients whose lives we judged to be immediately threatened by shock. As L-noradrenaline is a sufficiently powerful overall vasoconstrictor to be effective in doses ranging from 5 to 40 μg. a minute when used in the treatment of any peripheral vasomotor collapse (Swan, 1952), we ensured a sufficient dilution by adding 4 ml. of 1/1,000 L-noradrenaline bitartrate solution to a litre of isotonic solution either of 5% dextrose or of 4.3% dextrose in 0.18% saline, thus giving a drug strength of 4 μg. per ml. Normal saline as a vehicle was avoided in view of the danger of introducing excess of sodium ions into the circulation when heart failure existed or might supervene. Intravenous drip infusions were set up with one or other of these solutions, and preparations were made to continue the infusions for periods of a few hours to a few days. The concentration of drug necessary to keep the blood pressure at a chosen level varied greatly with each patient, but it was sometimes found that drip rates of more than 36 drops a minute were required. As this would entail giving a total infusion of more than three litres in 24 hours, the concentration of the L-noradrenaline bitartrate was increased as much as necessary—on one occasion to 64 ml. per litre—so as to be able to reduce the drip rate by the same factor. By this means the risk of circulatory overloading was abolished, although the control of the blood pressure by adjustment of drip rate became less sensitive.

In accordance with the main indication already mentioned, the use of L-noradrenaline infusion was considered whenever the systolic blood pressure was progressively falling in cardiogenic shock or when it was found to be 80 mm. or less for more than 24 hours, especially in the presence of a very small pulse pressure and oliguria. That we have been reluctant rather than anxious to employ this treatment is shown by the fact that two of our six patients were pulseless when the infusion was begun.

The presence of a nurse capable of measuring the blood pressure reliably was found to be essential. Throughout the whole period of the treatment vigilant attention had to be given to the drip rate, which might spontaneously vary with corresponding and perhaps dangerous fluctuations in blood pressure, which was generally kept between 100 and 110 mm. systolic. It was found that there was a direct and immediate relationship between drip rate and the blood pressure; with a turn of the regulating screw the pressure could be raised or lowered at will. On one or two occasions when the infusion was brought to an end the blood pressure fell abruptly; it therefore became our rule to discontinue the infusion by degrees while a close watch was kept on the blood pressure.

Case 1

A man aged 49 was admitted to hospital at 2 p.m. on June 16, 1952, on account of sudden very severe pain in the centre of the chest and vomiting. For three years he had had angina of effort; there had been cardiographic evidence of old antero-septal cardiac infarction, and the blood pressure was usually 140/90. He was extremely ill and shocked, and was drenched in sweat. The temperature was 97° F. (36.1° C.), and the heart sounds were distant. The systolic blood pressure was 60. Injections of morphine totalling ¾ gr. (50 mg.) were needed for relief of pain, and an intramuscular injection of 12,500 units of heparin was given. Although the condition improved during the day, the pressure during the following morning varied between 70 and 65 mm. systolic. In spite of intravenous injections of nikethamide, the pulse at the wrist disappeared, the extremities being cold and clammy.

An intravenous infusion of 20 oz. (570 ml.) of plasma failed to bring improvement. To a second similar quantity 4 ml. of 1/1,000 L-noradrenaline was added. Immediately this had started, the pressure rose to 100 and was maintained at 90 by an infusion rate of 60 drops a minute. Thereafter, the infusion was continued with 4.3% dextrose in 0.18% saline containing 16 ml. of 1/1,000 L-noradrenaline per litre; a drip rate of 36 drops a minute sufficed to keep the systolic pressure in the neighbourhood of 90 (Fig. 1). The condition of the patient remained critical, in spite of oxygen administration and maintenance of the drip throughout the day; on one occasion when it accidentally stopped the patient at once became pulseless. A pint (570 ml.) of plasma alone brought no improvement, but renewal of the L-noradrenaline infusion at once restored the pulse, while the pressure rose to 95 and later 115. The drip had to be maintained continuously for 48 hours, but when it was then discontinued the pressure fell slowly from 120 to 85, at which level it remained. An electrocardiogram showed antero-posterior infarction of the heart.

The patient made a gradual recovery in spite of temporary congestive heart failure, and he was discharged from hospital on July 27. Two months later he was readmitted in severe left ventricular failure, which in spite of every effort worsened and ended fatally on October 19, about four months after the onset.

Necropsy showed fibrotic scars of cardiac infarctions involving the posterior and lateral walls of the left ventricle and the anterior wall in the neighbourhood of the septum. The right coronary artery and the circumflex branch of the left coronary were occluded 2 cm. from the origin in each case.

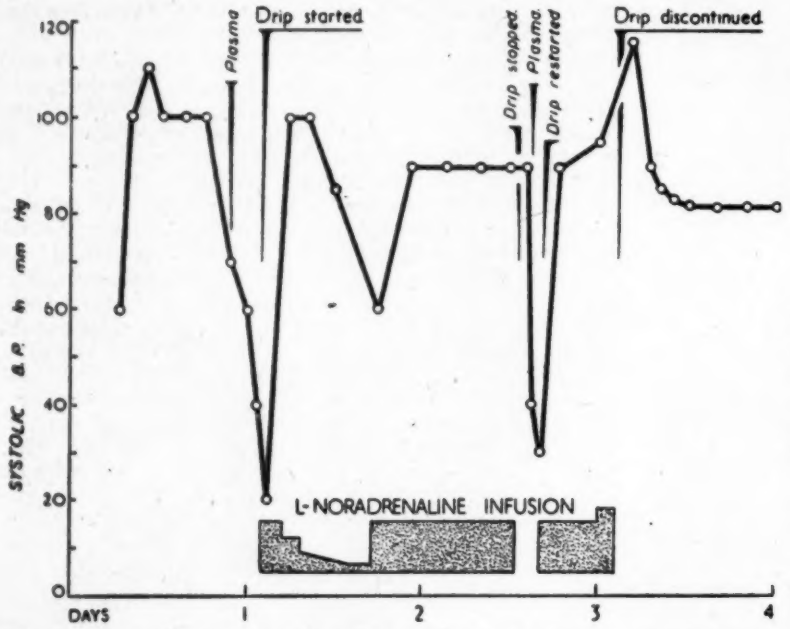

FIG. 1.—Graph showing rise of systolic pressure during intravenous infusion of dextrose–saline containing L-noradrenaline, 4 ml. 1/1,000 solution to the litre, in a patient with severe cardiac infarction and shock (Case 1).

Case 2

A woman aged 67 was admitted for an operation on her left hip. Clinical examination showed no cardiovascular abnormality save a blood pressure of 170/90. The operation was performed at noon on September 22, 1952. There had been little trauma or blood loss, but near the end of the operation she suddenly collapsed and became pulseless. Surgical shock was diagnosed, and an intravenous plasma infusion containing 4 ml. of 1/1,000 L-noradrenaline to the pint (570 ml.) was given, whereat the blood pressure became measurable at 80. On surgical grounds the infusion was changed to whole blood, and later to normal saline, but always with the same addition of L-noradrenaline, and at the rate of 40 to 60 drops a minute. Eleven hours after the start of the operation the patient regained consciousness. She had pain at the site of the operation, but nowhere else.

On the next day the condition had further improved. There was still no cardiac pain and the heart sounds were faint. Continuance of the L-noradrenaline–saline drip, now changed to 0.18% saline, enabled the blood pressure to be kept at about 100 mm. systolic, and the level could be raised or lowered at once by quickening or slowing the drip.

On September 24 an electrocardiogram revealed that the unsuspected cause of the collapse had been a large through-and-through antero-lateral infarction of the heart. The patient remained dependent on the L-noradrenaline infusion; although she was not breathless and the urinary output remained good, the sacrum and legs became oedematous. Fluid-balance charts revealed that 6 pints (3.4 litres) more fluid had been taken in than had been excreted in the previous 36 hours. This was remedied by quadrupling the concentration of L-noradrenaline and reducing the rate of the drip to 15 to 20 a minute. Heparin and biscoumacetate were then started. The L-noradrenaline administration had to be continued for five days, when a very gradual cessation was begun; any sudden reduction in drip rate was followed by an abrupt and dangerous fall of systolic pressure, so that the process of cessation took 72 hours to complete. The systolic blood pressure then remained at 85 mm., with a pulse of 100 a minute. During the next two months in hospital, the pressure fluctuated between 90/50 and 105/70, which was the reading on discharge. Seven months later there was no dyspnoea or angina, and the blood pressure was 105/70.

Case 3

A man of 53 was admitted at 6.30 p.m. on May 8, 1953, with a history of a sudden onset of severe retrosternal pain. He had vomited twice and sweated profusely. The extremities were cold, the temperature being 96.2° F. (35.7° C.), and the pulse regular at 36 a minute. The blood pressure was 80 systolic. The heart sounds were faint and the cervical veins engorged.

Electrocardiography confirmed the clinical presumption of complete A-V block and showed auricular fibrillation as well as patterns of an extensive posterior cardiac infarction. The blood pressure fell steadily in spite of general measures to combat shock, and one hour after admission it was 55 systolic, the patient looking as if about to die. The pulse rate was 40 a minute. As soon as an infusion of dextrose–saline containing 4 ml. of 1/1,000 L-noradrenaline per litre was started he looked better and uttered some words. At an infusion rate of 20 drops a minute the blood pressure rose swiftly to 80–115 systolic. Within 15 minutes of the infusion being started there was a sudden reversal to normal rhythm at 80 a minute (Fig. 2).

After one and a half hours of this treatment the drip rate was gradually slowed without fall of the blood pressure, and during the next two hours the L-noradrenaline concentration in the infusion was halved. It was discontinued after a total duration of just over three hours. During the next two months there was uninterrupted convalescence with improving effort tolerance. At a later examination the heart was found to be not enlarged and the pressure remained around 130/80.

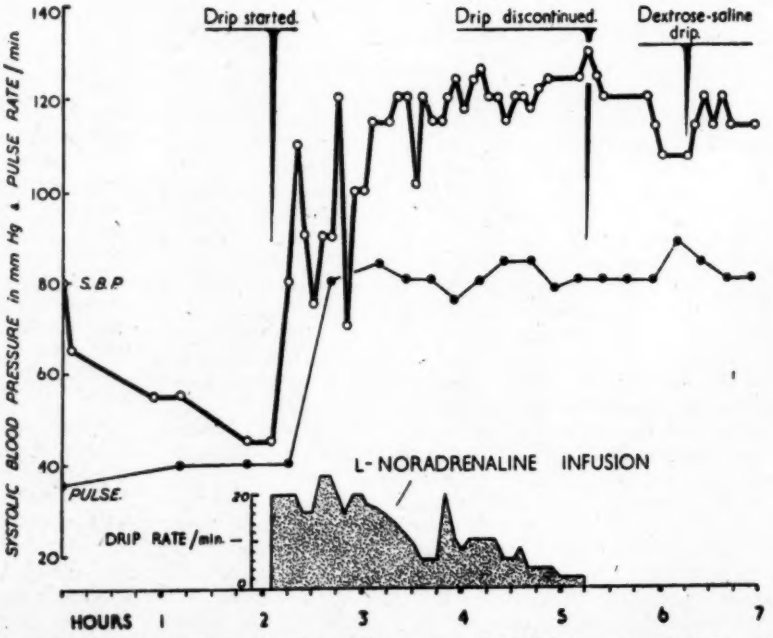

FIG. 2.—Graph showing rise of systolic pressure during intravenous infusion of dextrose–saline containing L-noradrenaline in varying concentration. Case 3, suffering from acute posterior cardiac infarction with initial complete A-V block and auricular fibrillation.

Case 4

A woman aged 73, a patient of Dr. D. I. L. Gleed, of Finchley, was seen in consultation on March 15, 1953. She had for nine years suffered from angina of effort, and had latterly been taking 50 trinitrin tablets weekly. At noon she was seized with an attack which caused collapse with loss of consciousness. She was grey and sweating with a weak pulse at 60 a minute. She vomited twice.

Examination six hours after the onset showed the patient still shocked, with a pulse of 72 and blood pressure 105/75. An electrocardiogram showed extensive postero-lateral infarction of the heart. Admission to hospital took place the same evening, when the pulse had quickened to 100 and the pressure had fallen to 90 systolic. Signs of congestive heart failure were developing, and there was pericardial friction to the left of the sternum.

At 1.30 a.m. that night renewed collapse occurred with sweating and unconsciousness; the systolic pressure fell to 50 and the pulse was hardly perceptible. At 2.5 a.m. an intravenous infusion of dextrose–saline containing 2 ml. of 1/1,000 L-noradrenaline per litre was started. Instantly the condition improved, the systolic pressure rising to 80 and later to 100. Throughout the day of March 17 the condition remained fairly satisfactory in that, despite sweating and chilliness of the extremities, the pressure was maintained at the same level by adjustment of the drip rate. Electrocardiography that evening showed that right bundle-branch block had now developed. The white cells numbered 31,200 per c.mm. During the following night the condition again became very grave, the pulse becoming weaker, with increasing signs of collapse. The drip rate was increased, but in spite of this and of an intravenous injection of theophylline with ethylenediamine the heart rate increased to 100 while the pulse became imperceptible. Death took place 66 hours after the onset of the illness.

Necropsy showed a recent infarction in the interventricular septum extending to the adjacent parts of the anterior and posterior walls of the left ventricle. The anterior part of the septum had become thinner, with the beginning of dilatation in this part of the ventricle. The remainder of the myocardium showed diffuse patches of fibrosis. Patches of calcified atheroma were found in both coronary arteries and their main branches. While the vascular lumen was in places much reduced, no occluding thrombus could be found.

Case 5

A woman of 75 was seen in consultation with Dr. Alan Strachan, of Sutton, on April 18, 1952, when she was in a state of cardiogenic shock. This had set in at 10 a.m. that day, about half an hour after an injection of morphine and atropine preparatory to dental extractions. It later transpired that three years previously a similar injection for gallstone colic had been followed within a few minutes by collapse, with pallor and a thready pulse. On that occasion there had been swift recovery after an injection of nikethamide, but in the present attack pain had developed around the trunk at the level of the diaphragm. The foot of the bed was raised and oxygen was given. The condition improved, but the pain persisted, later centring over the right upper quadrant of the abdomen.

At the consultation that evening there was pain across the lower part of the back with a bruised feeling in the upper part of the abdomen. The patient was shocked though not in distress; the pulse was regular at 64 a minute, and the blood pressure was 85 systolic. The clinical state did not permit thorough examination, but the heart sounds were heard softly at all areas, and there was no pericardial friction or gallop. There was no tenderness in the abdomen; arterial pulsation was felt readily in the feet. An electrocardiogram showed low voltage in standard leads, intraventricular conduction defect, and lateral subendocardial ischaemia. It was concluded that acute coronary insufficiency had followed a sudden severe fall of blood pressure as a result of abnormal sensitivity to an injection of morphine and atropine.

During the following day or two the condition fluctuated; the symptoms lessened but the blood pressure remained at 80 systolic. On April 22, four days after the onset, an intravenous drip infusion of dextrose–saline containing 4 ml. per litre of 1/1,000 L-noradrenaline was set up at 6 p.m. The blood pressure began to rise within a minute or two, and reached 90 after ten minutes. It then increased steadily to 120 at the end of 30 minutes. Slowing the drip was followed at once by a drop to 110, and this level was maintained without difficulty for four hours (Fig. 3). At the end of this time the systolic pressure was 105, and one litre of the infusion had been given. It was then discontinued.

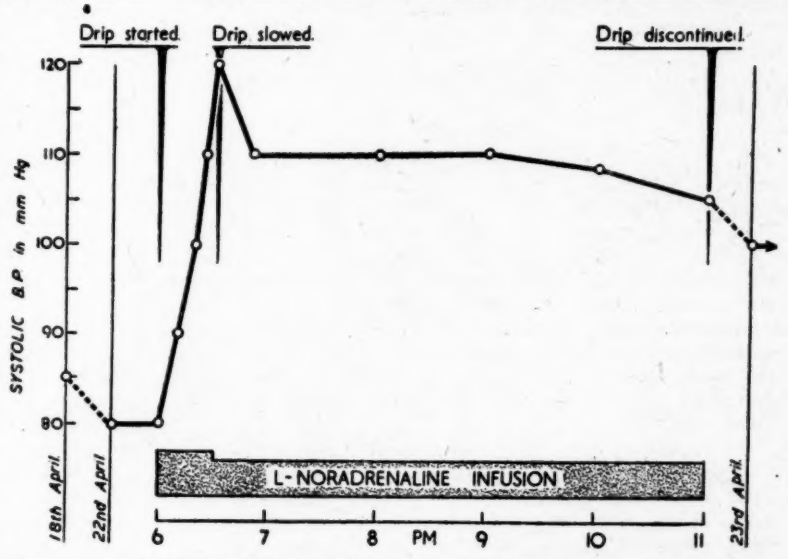

FIG. 3.—Graph showing rise of systolic pressure resulting from intravenous infusion of dextrose–saline containing L-noradrenaline started on the fourth day of cardiogenic shock due to acute coronary insufficiency (Case 5).

On the following morning the general condition had much improved and the pressure was 100. Three months after the onset the patient was up and about quietly, with a blood pressure of 110/75. The cardiogram showed regression of the patterns representing myocardial ischaemia. Radioscopy showed mild left ventricular hypertrophy, normal hilar shadows, and clear lung fields.

Case 6

A man of 61 who had been treated for cardiac infarctions in 1948 and December, 1952, was under periodic observation until, in the summer of 1953, he began to complain of dyspeptic symptoms, and a barium meal examination led to a diagnosis of carcinoma of the pylorus. Partial gastrectomy was performed by Mr. Norman Lake on August 20, with complete removal of a pyloric carcinoma. During the operation the patient never received less than 30% oxygen. Soon after the operation was started he became shocked and the pulse was faint and irregular. He was transfused with 2 pints (1,140 ml.) of blood, and after return to the ward the blood pressure was 130/90. During the next 36 hours the blood pressure fell gradually to 80/65, and he appeared to be moribund. It was judged that this illness was due to infarction of the heart, but cardiography could not be carried out at once. It was decided to give L-noradrenaline.

The infusion of dextrose–saline containing 8 ml. of 1/1,000 L-noradrenaline per litre was begun at a rate of 26 drops a minute. The blood pressure quickly rose to 110/85. In order to maintain this pressure it was necessary to raise

the drip rate to 40 drops a minute, and after 18 hours to double the concentration of L-noradrenaline and reduce the infusion rate from 40 to 30 drops a minute. At this stage a cardiogram showed antero-septal and postero-lateral infarctions. After a further six hours it was necessary to double the concentration again, and yet again seven hours later. The L-noradrenaline concentration was then 64 ml. per litre and the infusion rate 36 drops a minute. Over the next 12 hours the blood pressure was maintained at 110/85 with no further increase in concentration of the drug, and with a decrease in the rate of infusion to 24 drops a minute. The patient then suddenly developed a pulmonary embolism and died at 1.30 a.m. on August 25, one and a half hours after the onset of this complication.

The necropsy confirmed that there was a massive pulmonary embolism involving the whole right lower lobe. The anastomosis of the stomach remnant to the jejunum was intact and no evidence of secondary neoplastic deposits was found. There was severe widespread atheroma of the coronary arteries. A large antero-septal infarction and a small postero-lateral infarction of the heart were present. There were also three old infarctions involving the posterior and lateral walls of the heart. In the left ventricle a great part of the muscle had been replaced by fibrotic tissue.

Discussion

The shock in myocardial infarction needs no special treatment if it is slight. It is upon the treatment of severe and continuing cardiogenic shock that controversy has centred. While some clinicians have employed oxygen, infusions of hypertonic glucose solutions, and stimulants such as nikethamide, these methods have not given constant or convincing results. There has naturally been a temptation to use pressor substances such as adrenaline and ephedrine, and, although they have been advocated in the past by Fishberg (1937), they have been generally condemned on account of the risk of inducing ventricular fibrillation (Eggleston, 1947; Wood, 1952).

The introduction of noradrenaline, and particularly of L-noradrenaline, the optical isomer which acts mainly upon blood vessels, has revived interest in the use of pressor substances in shock. This compound is the most powerful overall vasoconstrictor known and it lacks many of the pharmacological actions that have rendered adrenaline and ephedrine dangerous in cardiac infarction. Thus, in contrast to adrenaline, it does not increase the rate of the heart or the cardiac output; this is the result of reflex vagal cardioinhibition, for L-noradrenaline stimulates mildly, but definitely, the isolated mammalian heart and the heart of the human under the influence of atropine. Also, whereas adrenaline raises the systolic pressure by its profound cardiac effects and hardly influences or actually lowers the diastolic pressure because of muscle vasodilatation, L-noradrenaline increases both systolic and diastolic pressure as a result of the marked generalized vasoconstriction (Goldenberg *et al.*, 1948). Moreover, Reale *et al.* (1950) have shown that, in the healthy subject, intravenous L-noradrenaline does not increase the oxygen consumption, as does adrenaline. Additional support for the use of this substance in shock due to heart disease comes from Burn and Hutcheon (1949), who have shown that L-noradrenaline is a coronary vasodilator in dogs and cats, but species differences exist and no work has been found on the action of the drug on the adult human coronary artery.

In experimental myocardial ischaemia in dogs produced by tying a coronary artery, Corday *et al.* (1949) demonstrated the harmful effects of hypotension on the infarcted zone and showed that such effects could be reversed by correcting the hypotension. In addition, Sayen *et al.* (1952) have shown that an L-noradrenaline infusion causes a rise in oxygen tension in the ischaemic zone, an effect greater than that produced by pure oxygen inhalation, while no ectopic beats or other arrhythmias were observed during the course of the infusion. On the other hand, Wiggers (1952) has pointed out that such experiments have been performed on dogs in which intercoronary anastomoses are better developed than in man, and he groups noradrenaline with adrenaline and ephedrine as potentially dangerous in myocardial infarction owing to the increase in the work of the heart and the risk of ventricular arrhythmias.

After weighing all such clinical and experimental evidence, it remains clear that even serious risks might be accepted when the blood pressure in cardiogenic shock is progressively dropping, when the pulse is disappearing, and death wellnigh at hand.

Some work on the use of L-noradrenaline in the shock attending myocardial infarction in man has already been published. Miller and Baker (1952) employed this treatment in seven such patients. A rise of blood pressure was produced in four and in no instance was there any arrhythmia. Six of the patients died. The criterion for use in these cases was a systolic blood pressure of 80 or less continuing for four hours, and they concluded that the results might have been better had infusion been started earlier. Maintenance of infusion until the improvement in the circulatory state was established, and gradual rather than abrupt cessation was advised. More favourable results have been reported by Kurland and Malach (1952), who treated with L-noradrenaline 14 patients suffering from shock due to cardiac infarction. In 12 cases there was a significant pressor response, but the ultimate results were disappointing, as five died from 1 to 41 days after recovery from the state of shock and only four ultimately survived. No arrhythmias that could be attributed to the infusion were observed, although these workers recorded intense venous spasm, phlebitis, and ulceration of the skin at the site of the infusion as occasional complications.

Although our series of six cases is a small one the results are encouraging, since four of these patients survived for four months or more. Three of them were still alive at intervals of six to thirteen months after infarctions which caused grades of shock so severe and prolonged that death appeared to be imminent. In no case did L-noradrenaline cause harm. In spite of the increase in systemic and pulmonary resistances heart failure was never induced by the treatment.

In this grave state of cardiogenic shock there are two elements; the shock and the underlying myocardial injury. Study of our cases endorses what must have been the clinical impression of many—that the degree of shock is not necessarily proportional to the extent of the infarction. If shock is severe and the lesion is gross, then a fatal issue may be determined by the extreme disorganization of the heart. But when, as is sometimes the case, a lesser injury is attended by grave shock, then there is the possibility of recovery and subsequent reasonably good myocardial function, if the critical phase of shock can be surmounted, as exemplified in three of our cases. In the three patients who have died, necropsies have revealed multiple infarctions, old and new, representing a high degree of myocardial damage.

Summary

Six patients in severe shock due to cardiac infarction have been treated by intravenous infusions of dextrose–saline containing L-noradrenaline (levophed). In all of them a fatal issue appeared imminent or probable, the systolic blood pressure falling to levels between 45 and 80, and in two instances the wrist pulse disappearing.

In each case the start of the infusion was followed at once by clinical improvement, the systolic pressure rising to levels between 90 and 100, while the pulse again became palpable; where consciousness had been lost it was regained.

Two patients who had had previous infarctions responded in this way to the infusion, but died within three and four days, recent as well as old infarctions being proved at necropsy.

The remaining four patients made good recoveries after discontinuance of the infusions. Although one died of congestive heart failure four months after the cardiac infarction, the other three were alive and active at intervals ranging from six to thirteen months afterwards, their lives apparently having been saved by the treatment.

The criteria for infusion of L-noradrenaline are discussed and the methods and precautions necessary for its use described.

We are indebted to Dr. N. S. Plummer and Mr. David Trevor for allowing us to study their patients (Cases 3 and 2); to Dr. Alan Strachan, of Sutton, for his help in the clinical observations and treatment of Case 5; to Dr. D. I. L. Gleed, of Finchley, for her initial records of Case 4; to Dr. W. Evans for the pathological reports on Cases 1 and 4; and to Dr. H. Neville Stafford for the necropsy report on Case 6.

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ACUTE DISSEMINATED ENCEPHALOMYELITIS AND ACUTE DISSEMINATED SCLEROSIS

RESULTS OF TREATMENT WITH A.C.T.H.

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The treatment of seven cases of acute disseminated encephalomyelitis with A.C.T.H. was reported in a previous paper, in which the theoretical basis for trial of the drug was discussed (Miller, 1953). The results of treatment were held to be suggestive enough to warrant further trial. Three further cases have now been treated, and they are briefly reported below.

We have also used A.C.T.H. in the treatment of seven patients with acute exacerbations of disseminated sclerosis. Glaser and Merritt (1952) have already reported on the use of the drug in disseminated sclerosis. They treated 33 cases of the disease, giving 80 to 100 mg. daily during a course of 14 days' duration. These were chronic cases, and none had experienced significant remission during the three years preceding treatment, or since the onset of the disease in cases of less than three years' duration. Twelve patients showed significant improvement. The syndromes benefited were spastic-paretic, cerebellar-ataxic, bladder dysfunction, and visual impairment of recent origin. Oculomotor disorders, sensory impairment, and reflex changes remained unaffected. The effects observed appeared during the course of drug administration and rarely persisted for more than seven to fourteen days after the end of treatment. In most cases the disease later resumed its usual course, though these authors believed that subsequent maintenance treatment with 75 to 150 mg. of cortisone daily might possibly retard its progression. They considered that the beneficial effects of the drug represented "secondary physiological phenomena due to the hyperadrenal state," whether produced by interference with abnormal immunological reactions in the central nervous system, suppression of inflammatory and connective-tissue responses, or the effect on nervous excitability of chemical changes related to the profound metabolic disturbance which A.C.T.H. is known to produce. A somewhat similar transitory improvement in cases of established disseminated sclerosis has been reported by Fog (1951).

We have, however, restricted the experimental use of A.C.T.H. to patients with a recent acute exacerbation of unequivocal established disseminated sclerosis. All cases had recently developed an acute neurological episode with some objectively assessable focal disability, either a fresh manifestation of the disease or the sudden aggravation or reappearance of a previous symptom. No patient was showing any sign of spontaneous improvement when treatment was begun, and progressive deterioration was evident in several. It seems reasonable to believe that the onset of an acute neurological episode of this nature signals the development of fresh plaques in the central nervous system. Although there is no general agreement on the pathogenesis of disseminated sclerosis, nor indeed on the histopathological changes present in recent lesions, it seemed justifiable to make a trial of A.C.T.H. in such cases.

We had found apparent improvement in acute disseminated encephalomyelitis, which shows several clinical and pathological similarities to disseminated sclerosis. Moreover, if an abnormal immunological reaction were responsible for such exacerbations (Pette, 1942) there are theoretical grounds for believing it might be aborted by A.C.T.H. There are similar grounds for believing that A.C.T.H. might also lead to the resolution of the acute inflammatory reaction which was considered by earlier authors—for example, Marburg (1906, 1942)—to be the basis of acute episodes of disseminated sclerosis. If, however, the initial change of the disease is demyelination, possibly as a result of enzymatic disorder (Lumsden, 1951), A.C.T.H. would be unlikely to have any effect once the process had begun, although such a view of the disease does not preclude the possibility that long-term administration of the drug might possibly prevent the development of fresh lesions.

It was felt that by selecting our cases on the above lines it would be possible to make an initial assessment of the effects of the drug on a relatively small number of cases, with a view to a more extended trial if the results were suggestive enough to justify this. It may be remarked that the collection of cases satisfying these criteria proved quite unexpectedly difficult.

In all cases of acute disseminated encephalomyelitis and disseminated sclerosis treated, 25 mg. of A.C.T.H. was given intramuscularly every six hours, usually for a period of five days. Repeated eosinophil counts were made, but in all the cases reported adequate adrenal response was obtained with this dosage.

Acute Disseminated Encephalomyelitis

The three additional cases of acute disseminated encephalomyelitis treated with A.C.T.H. comprise one case of special interest—an example of encephalomyelitis occurring during the course of acute rheumatic fever—and two patients suffering from encephalomyelitis following measles.

Case 1

Encephalomyelitic illness arising during the course of acute rheumatic fever in an 11-year-old boy of low average intelligence. Rapid recovery, beginning within 12 hours of administration of A.C.T.H.

Six weeks before his acute neurological illness this boy developed a febrile sore throat with muscle pains. This cleared up within a week but left him off colour, eating badly, and losing weight. Three weeks after the onset of the initial infection he developed a transient coalescent multiform erythematous rash, and a week later an acute polyarthritis with which he was admitted to hospital. At this time he was toxic, but only occasionally febrile, with a pulse rate of 122, a systolic apical murmur, triple rhythm, and partial auriculo-ventricular block with occasional dropped beats. During two weeks in hospital the joint pains were greatly relieved by salicylates, there was only an occasional spike of fever, and the E.S.R. fell from 125 to 41 mm. in the hour (Westergren). However, the child remained ill, and a continuing carditis revealed itself by persisting cardiographic signs, an increasingly loud murmur, and an episode of probable pleuropericardial friction.

Seventeen days after admission to hospital he was observed to be drowsy, and within thirty hours passed through stages of deepening stupor, lighter during the day and deeper nocturnally, to become almost unrousable.

Examination revealed slight neck stiffness, unequal sluggish pupils, spontaneous nystagmus, and a generalized increase of deep reflexes with extensor plantar responses. Within the next six hours he became profoundly hypotonic, with absent deep reflexes, and entirely unresponsive even to painful stimuli. The pressure and composition of the spinal fluid were entirely normal. An E.E.G. showed diffuse slow activity, chiefly in the delta range.

At this stage, 36 hours after the onset of neurological symptoms, he was given 50 mg. of A.C.T.H. followed by four injections of 25 mg. at six-hourly intervals. Improvement was evident within twelve hours. The patient was easily rousable, answered questions, and took food. Neck stiffness was less, the pupils were equal but sluggish, muscle tone was normal, and plantar responses remained extensor. Neurological improvement from this time was progressive. For three days the child was unduly drowsy at night, but at the end of this time symptoms and signs had entirely disappeared and the plantar responses were flexor.

Following this the child developed several syncopal attacks accompanied by extreme bradycardia, with a pulse rate as low as 38, which were improved by ephedrine. The E.E.G., however, showed progressive improvement, though the rheumatic process continued in a subacute form, and within seven days an apical diastolic murmur and involuntary movements typical of Sydenham's chorea made their appearance.

Case 2

Measles encephalitis in a boy of 10. A.C.T.H. given from the seventh day of the neurological illness. Improvement slow but progressive to complete recovery.

Four days after the appearance of a typical measles rash, when this previously healthy child appeared to have recovered, he suddenly became quiet and apathetic. He lay almost motionless thereafter, refusing food. On the third day he became mute and his legs stiff. On the fourth he developed retention of urine, and examination on admission to hospital showed him to be flushed and restless, with meningism, general hyperreflexia, extensor plantar responses, and a normal spinal fluid. Twelve hours later he was barely rousable, and was febrile—99.6° F. (37.6° C.). The signs were unchanged, except that his stupor was deeper and the legs had become flaccid and the arms spastic.

A.C.T.H. was given at once. Twelve hours later he was more easily rousable but remained mute. Twenty-four hours after the first dose he was making semi-purposive movements with his arms and meningism had decreased. Twenty-four hours later the tendon reflexes became normal, and during the next few days tone in the limbs varied from hour to hour. Improvement from this time was progressive but very slow, and it was not until the fifteenth day of the illness (three days after completion of his five-day course of A.C.T.H.) that facial expression became normally mobile. Two days later the plantar responses had become flexor, and 48 hours after this he began to talk. He remained emotionally labile and inattentive for at least three weeks, and convalescence was prolonged.

Case 3

Severe measles encephalitis in a girl of 3½, with myoclonus, coma, hyperpyrexia, and death within four days of onset, after 36 hours' treatment with A.C.T.H.

Five days after the appearance of measles this child was noticed to be unusually quiet and to have apparent brief lapses of consciousness. During the next two days her condition deteriorated, with increasing drowsiness and occasional muscle-twitching. On examination at this time she was deeply stuporous, but resisted violent stimuli. She was febrile—100.2° F. (37.9° C.)—and generally hypertonic, with hyperreflexia, absent abdominal reflexes, and extensor plantar responses. Repeated myoclonic twitching was present in the left hand and foot. There was no meningism and the spinal fluid was entirely normal. A.C.T.H. and suitable sedatives were administered at once. Twelve hours later stupor had deepened to an unresponsive coma. Convulsive twitching was bilateral and continuous, shifting from one group of muscles to another. During the subsequent 24 hours these movements ceased except in both eyelids, all four limbs became flaccid, and death occurred in hyperpyrexia after an illness of four days' duration. Permission for necropsy was refused.

Comment

Cases of acute disseminated encephalomyelitis in association with rheumatic fever similar to Case 1 have been described by van Bogaert *et al.* (1932). Although these illnesses are clinically similar to para-infective encephalomyelitis of more familiar types, a rather different pathological basis has been described by Costero (1949), who found a diffuse cerebral angiitis of "hyperergic" type in fatal cases of rheumatic fever both with and without cerebral symptoms.

By comparison with Case 1 the two cases of measles encephalitis (Cases 2 and 3) were disappointing, especially as success has already been claimed for the use of A.C.T.H. in this condition (Ligterink, 1951). In Case 2 treatment was not begun until the fifth day of the disease, and, although admittedly the patient gradually recovered from this time onwards, there was no dramatic response to A.C.T.H.: the disease ran a course with which we are familiar in untreated cases, convalescence being protracted. Case 3 deteriorated rapidly in spite of treatment. This may well be considered to fall into the second group of cases which we have considered on theoretical grounds unlikely to respond to treatment—"the rapidly fatal encephalomyelitic illness of which the pathological basis is a diffuse cerebral purpura."

Disseminated Sclerosis

Eight acute episodes of disseminated sclerosis in seven patients have been treated with five-day courses of A.C.T.H., as shown in the Table. Each case satisfied the criteria already described. We had hoped that A.C.T.H. might cause rapid resolution of the acute lesions of the

Details of Cases of Disseminated Sclerosis

Case	Age and Sex	Duration of History	Apparent Provoking Factors	Clinical Features of Acute Episode	Background Disability	Results of Treatment
A1	27 M	2 years	0	Spastic weakness and paraesthesiae in right hand for one week	Spastic paraplegia. Difficulty in micturition. Ataxia	Disappearance of acute symptoms. Relief of spasticity and bladder disorder. No change in reflexes
A2		2½ ,,		Exacerbation of weakness of legs	As above	Relief of bladder symptoms only. Euphoria
B	38 M	10 ,,	0	Acute exacerbation of spastic paraplegia 6 weeks before. Later widespread painful paraesthesiae	Spastic paraplegia. Dysuria. Ataxia	Decrease of long-standing spasticity in right leg. No change in reflexes. Euphoria
C	49 M	6 months	0	Ataxia of gait, with flexor spasms in legs	Bilateral pyramidal signs. Paraesthesiae. Little weakness	No change. Euphoria
D	42 F	17 years	Febrile sore throat one week before	"Useless" left arm for 4 days	Spastic paraplegia. Dysuria. Ataxia	No change
E	33 M	9 ,,	0	Increasing spastic paraplegia and paraesthesiae for two days	Nil (complete previous remission)	,, ,,
F	31 F	16 ,,	Common cold 23 days before	Spastic tetraplegia developing during a few hours	Spastic weakness of right leg	Aggravation of symptoms during treatment
G	20 F	4 weeks	0	Increasing weakness of legs for three days. Optic neuritis	Nil	Aggravation of symptoms during treatment. Euphoria (subsequent course of illness confirmed diagnosis)

disease, with concomitant improvement in symptoms. It seemed possible that the control of acute episodes might lessen permanent damage to the nervous system and so improve both immediate and long-term prognosis.

The results were, however, profoundly disappointing. The first patient treated appeared to respond (Case A1). His most recent symptoms—spasm and paraesthesiae in the right hand—resolved during the course of treatment, while bladder control was improved and spasticity reduced without change in the reflex signs. Several weeks later, however (Case A2), a second acute episode in the same patient was characterized by a rapidly developing exacerbation of paraplegia, ataxia, and recurrent bladder symptoms. This exacerbation proved entirely unresponsive to a similar course of A.C.T.H., with the sole exception that dysuria was again apparently improved. In no other case was improvement in acute symptoms observed. One other patient (Case B) showed a definite decrease in long-standing spasticity, while his more recent symptoms remained unchanged. Case G had acute visual impairment, but became dramatically worse during the five days of treatment. The one really striking effect of A.C.T.H., observed in four patients, was the rapid development of marked euphoria, sometimes with extravagant claims of subjective improvement in function for which no objective basis could be found. This euphoriant action is well known, and makes clinical assessment difficult, for a cheerful patient may make much more effort than a depressed one in such tests as those for muscular power.

It will be seen that the only definite benefits derived by these patients are among those enumerated by Glaser and Merritt—decrease in spasticity and improved bladder function. We must conclude from this small group of patients that A.C.T.H., given in physiologically adequate dosage over the course of five days, has no specific effect on the acute manifestations of disseminated sclerosis. There seems no reason to believe that cortisone would be any more effective. The place of A.C.T.H. or cortisone in maintenance treatment, with the aim of preventing fresh lesions, remains to be established.

Discussion

In all we have now treated 10 cases clinically diagnosed as acute disseminated encephalomyelitis with A.C.T.H., and the results are on the whole distinctly encouraging. Two cases followed measles, two varicella, and three respiratory infections; one occurred in association with acute rheumatic fever, and one after body-chilling, while the remaining illness developed apparently spontaneously (subacute necrotic myelitis). In seven patients marked improvement occurred during five-day courses of the drug, and in five instances quite unequivocal clinical improvement appeared within 12 hours of the initial injection of A.C.T.H. The two complete failures were in subacute necrotic myelitis and in the very acute measles encephalitis described above (Case 3)—cases which on theoretical grounds would seem very unlikely to respond. These illnesses tend, of course, to spontaneous and often dramatically rapid recovery, and we cannot yet be certain that the course of the illnesses was in fact altered by the administration of A.C.T.H. Nevertheless the evidence in favour of this view is very suggestive, and may perhaps be regarded as more so when it is observed that improvement occurred within twelve hours of instituting therapy in four of the six patients in whom treatment was instituted within forty-eight hours of the onset of neurological symptoms, but in only one of the four cases in which the symptoms were of longer duration. Such rapid improvement in early cases is entirely in keeping with the hypothesis on which this therapy is based (that acute disseminated encephalomyelitis represents a neurological analogue of urticaria or "anaphylactoid purpura"), and is surely the reverse of what might be expected did our case records represent the natural history of encephalomyelitic illnesses unaffected by therapy.

Consideration of these results suggests two further approaches. Clinically it would be of interest to observe the effects of the more rapidly acting intravenous cortisone or compound F on the severe acute encephalitic illnesses in this group. Secondly, observations on the possible therapeutic action of cortisone or A.C.T.H., as opposed to their verified prophylactic effect, in experimental "allergic" encephalitis might yield further information on what might be hoped for in dealing with the disease in man.

It appears, however, that while most cases of acute disseminated encephalomyelitis show definite clinical improvement during a five-day course of A.C.T.H., a similar course of treatment produces no effect on acute episodes of disseminated sclerosis. This finding permits of two possible interpretations. Either acute disseminated encephalomyelitis responds to A.C.T.H. and acute disseminated sclerosis does not, or neither disease is influenced by the treatment and the differences observed are inherent in the natural history of the two syndromes. Although we believe the second interpretation to be the less likely, it cannot be doubted that the two conditions are distinct. It has never been suggested that post-exanthematous or post-vaccinal encephalomyelitis develops into disseminated sclerosis. Nor have we ever encountered in disseminated sclerosis that dramatically rapid spontaneous resolution of gross neurological signs within hours or days which is a common occurrence in the patient with acute disseminated encephalomyelitis. Furthermore, follow-up studies of apparently spontaneous acute disseminated encephalomyelitis have shown that recurrence is unusual and that the prognosis

after survival of the acute illness is good (Thygesen, 1949; van Bogaert, 1950; Miller and Evans, 1953). That the ultimate prognosis of recovered neuromyelitis optica, which we regard as a variant of acute disseminated encephalomyelitis, is similarly favourable has been clearly shown by Scott (1952).

The differentiation of acute disseminated encephalomyelitis from acute disseminated sclerosis is therefore of much more than academic importance, but it may be very difficult in the acute stage. Both illnesses show signs of disseminated lesions in the neuraxis, both tend to occur in young adults, and both often follow non-specific infections, especially of the respiratory tract. In our experience the diagnostic criteria offered by McAlpine (1931) are invaluable, but the need for further study is demonstrated by the following recent case.

Seven weeks before admission to hospital a young man of 19 developed an acute influenzal illness, epidemic at the time in the Army camp in which he was serving, and associated in his case with quite severe pain in the left eye which lasted for three days. He recovered completely from his symptoms within a week, but seven days later vision in the left eye suddenly became blurred. Examination at this time revealed a unilateral retrobulbar neuritis with papillitis; there were no abnormal signs elsewhere. Sight in the left eye became normal within a week and the patient remained well until one month later, when he developed acute backache, followed by weakness and stiffness of the legs, constipation, and retention of urine. Examination at this time revealed some pallor of the left optic disk, nystagmus at the extremes of lateral gaze, and signs of a partial transverse lesion of the spinal cord in the mid-dorsal area, with loss of proprioceptive sensation in the feet and of impairment of superficial sensibility to the seventh thoracic dermatome. The spinal fluid contained 73 lymphocytes per c.mm., but was otherwise normal. Improvement from this lesion was rapid, and a mild spastic paraparesis with some left optic atrophy was at the time of writing the only evidence of his illness.

Was this a case of rapidly healing biphasic encephalomyelitis, showing some similarity to the syndrome of neuromyelitis optica, and with only slight danger of recurrence? Or must it be labelled as disseminated sclerosis, with all the sinister implications of that diagnosis? The answer to such problems seems less likely to depend on further refinements of clinical diagnosis than on the development of such ancillary aids as are suggested by the immunochemical studies of Kabat *et al.* (1948) or the refined colloidal gold reaction described by Lange and Harris (1949), which may ultimately furnish diagnostic instruments of critical importance.

Summary

Three further cases of acute disseminated encephalomyelitis personally treated with A.C.T.H. are reported, bringing the total of cases treated to 10. In seven patients marked improvement occurred during five-day courses of the drug, and in five of these unequivocal clinical improvement was observed within 12 hours of the initial injection of A.C.T.H. The two complete failures were in cases of subacute necrotic myelitis and catastrophic measles encephalitis. Improvement occurred within 12 hours in four of the six cases in which treatment was instituted within 48 hours of the onset of neurological symptoms, but in only one of four cases treated later in the course of the illness. This finding is regarded as a further indication that the course of the illness was favourably influenced by treatment.

Similar courses of A.C.T.H. were given during eight acute exacerbations of disseminated sclerosis in seven patients. Although euphoria was often present and improvement in chronic spasticity and bladder dysfunction occasionally observed (in keeping with results previously reported), acute symptoms showed no improvement comparable to that seen under similar conditions in acute disseminated encephalomyelitis.

The importance and the occasional difficulty of distinguishing between these two clinically similar but biologically distinct acute neurological syndromes are discussed and illustrated.

We wish to thank practitioner and consultant colleagues in Region No. 1 for their kind co-operation in referring cases for treatment, and the Medical Research Council for a supply of A.C.T.H.

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CONSERVATIVE SURGERY IN THE TREATMENT OF ULCERATIVE COLITIS

BY

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There is no doubt that the modern improvements in ileostomy bag design have relieved an ileostomy of some of its terrors, but, in spite of this and the reports of many patients who have returned to most of their former activities, it would be idle and false to pretend that the prospect of an ileostomy for the rest of life is one that does not bring dismay and gloom to those of finer sensibility. Many patients for whom an ileostomy is contemplated or performed are in their youth and in their early married and home life, and few can believe that such distortion of the normal channels of evacuation is likely to prosper that alliance and that household. It is surely right that surgical opinion should not accept the inevitability of permanent ileostomy combined with total colectomy and excision of the rectum as the routine surgical treatment of the disease without the fullest exploration of more conservative methods. Devine and Devine (1948), in a series of cases, have put forward a technique whereby the rectum is preserved and continuity of the intestinal track re-established; and Corbett (1952), working along similar lines, has reported successful cases. Both of these methods entail the full discharge of ileal content through an ileostomy that is retained for varying periods of time, but the method of continuity suggested in this paper, dependent as it is upon immediate ileo-pelvi-rectal anastomosis, carries no such disadvantage.

Those antagonists of any attempt to preserve rectal function contend that the inflammatory changes present in the rectal mucosa continue in spite of removal of the rest of the colon and that the mucosa is unable to withstand the proteolytic effect of the ileal contents which are poured into it. Moreover, they regard the possibility of cancerous change in the remaining portion of the bowel as a very real one, and in the event of existing

complications of the disease being present, such as arthritis or pyodermia, they believe that these are not cured so long as a portion of the large bowel remains.

In certain cases, at least, it is doubtful whether these fears are real, and it is still more dubious whether they should prevent the surgeon from an attempt at restoration of continuity of the bowel. Devine and Devine have described the regression of the acute inflammatory change in the rectum, once its connexion with the colon has been severed, so that the mucosa returns practically to its original state, and my own experience supports this view. That the rectum and anal canal can withstand the proteolytic action of small-intestinal content has been proved to my satisfaction by my experience with anastomosis of the small intestine to the rectum for other conditions (Aylett, 1951, 1952), so that this consideration, too, cannot be held as a bar to attempts at functional restoration.

Suitable Cases

In the type of case upon which a conservative operation is proposed, the possibility of carcinomatous change in the remaining rectum is not a real one. Counsell and Dukes (1952) have shown that in ulcerative colitis cancerous changes occur either in association with a dense fibrous-looking stricture or as a result of malignant changes supervening in true adenomata. The common inflammatory pseudo-polyps and oedematous mucosal tags are not premalignant and may disappear completely with the amelioration of the disease. Where the rectum is studded with true adenomata the nature of which will be revealed by preoperative biopsy examination, or where, in the course of sigmoidoscopic examination, stricture formation is identified in the portion of the bowel it is proposed to retain, any consideration of conservative surgery must naturally be abandoned in favour of an ileostomy with complete removal of the colon and rectum. In the absence of such changes, even though the typical acute inflammatory appearances with pseudo-polyps are obvious, I consider that the operation should be planned with a view to retention of the rectum.

Of the five cases reported below, one had a severe pyodermia. In this case at least, the condition resolved completely, and the return of the rectal mucosa to a normal appearance encourages us to believe that other extra-bowel lesions may resolve in a like manner, with a conservative operation retaining rectal function.

It is not within the scope of this paper to consider the numerous indications for surgical intervention in this disease, but if conservative surgery is to be contemplated it is essential that stricture formation in the rectum and the lowermost part of the colon shall be absent. In dealing with the case that is under prolonged medical treatment the closest co-operation between physician and surgeon is therefore essential, so that operation shall not be delayed until this complication has developed. It is only by sigmoidoscopic examination that the early stage of bowel changes likely to go on to stricture formation can be recognized, and this investigation must therefore be carried out at frequent intervals throughout the patient's illness. Distensibility of the rectum and colon is at all times diminished in cases of ulcerative colitis, as the normal elasticity of the bowel is reduced by the oedema and inflammatory changes that affect all its layers, but the start of actual stricture formation is suggested when the sigmoidoscope feels held up or gripped at any level of the bowel within the scope of the examination, or if the wall feels thickened and unduly resistant. In all such cases medical treatment should be abandoned in favour of surgery, as, if the former is prolonged, stricture formation will develop and retention of a functioning rectum will be impossible.

A conservative operation will also be out of the question when perirectal abscess and fistula formation is present, but if the disease is regarded as one in which both physician and surgeon have an equal interest, and one in which operation does not carry the inevitability of permanent ileostomy, then the disease is unlikely to be allowed to reach the advanced stage before surgery is undertaken. Finally, the prospect of the retention of rectal function, by overcoming both the patient's disinclination to submit himself to an operation which is to result in a permanent ileostomy and the physician's natural reluctance to advise such a procedure until the very last, may help to avoid the "Belsen" type of case in which any operation must carry an appreciative mortality.

Operative Technique

The abdomen is opened through a left paramedian incision and the ileum divided close to the caecal valve. Both free ends are closed, and the proximal end is anastomosed to the pelvi-rectal region of the colon by side-to-side anastomosis.

The colon is then divided about 2 in. (5 cm.) above this site and the free ends are brought out on to the skin surface in the left iliac fossa (Fig. 1).

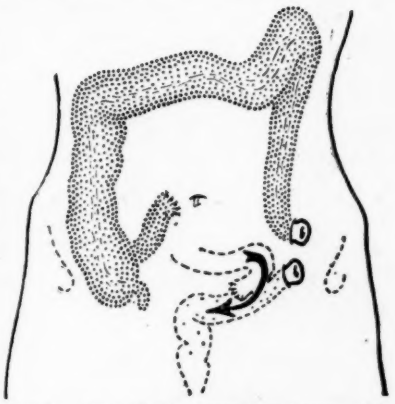

FIG. 1.—The final altered anatomy, with the distal ends of the colon exteriorized.

The patient is thus left with an end of the colon, a little above the anastomosis, opening on to the surface of the abdomen. This provides a safety-valve effect, so that any pressure, the result of the accumulation of intestinal content or flatus in the rectum, which might be sufficient to break down the anastomosis between the ileum and the colon is prevented from developing, as the contents will discharge through the colostomy before enough tension to produce damage has been built up. In actual practice, although considerable quantities of flatus are passed, the amount of ileal content that escapes on to the abdominal surface is not great and has not been sufficient to produce excoriation of the skin. Nevertheless, I feel sure that the absence of any suggestion of a leakage in my cases at the anastomotic site has been due to the safety-valve effect of this colostomy, and that an intraperitoneal anastomosis carried out through grossly diseased bowel wall without this device would be fraught with great danger of leakage. The idea of decompression of the bowel by this method was first introduced by Muir (1947), who employed the technique when carrying out a right hemicolectomy.

In two of the five cases recorded below the condition of the patient at the completion of the ileo-pelvi-rectal anastomosis was good enough to enable the colectomy to be carried out at the same operation, so that only the distal free end of the colon was drawn out on to the surface of the abdomen. The general condition of most patients, however, would not permit of this, and the colectomy must be delayed until sufficient improvement has been achieved as a result of the ileocolostomy.

Closure of the safety valve some three to four weeks after the initial operation is the next step in the planned treatment of the condition. By this time the anastomosis will have united soundly, and there is then no need of the safety-valve effect. Moreover, it is best that this should be closed before the abdomen is reopened to remove the colon, as the risk of faecal contamination of the abdominal wound is thereby reduced. In Case 5 of the series reported, however, it was necessary to carry out the colectomy before the closure of the colostomy, as, after a period of great

improvement in the child's general condition following the first operation, deterioration began as a result of constant haemorrhage from the isolated colon. Colectomy was the final stage of operation in the remaining two patients. (Fig. 2.)

The progress of all patients after the ileocolostomy has been absolutely smooth and there has been no anxiety with regard to saline or fluid unbalance. Until a return of peristalsis, intravenous therapy has been continued, but, apart from an immediate post-operative blood transfusion, no continuance of this form of therapy has been necessary, even in those who, prior to the operation, needed weekly blood transfusions to maintain a normal blood picture.

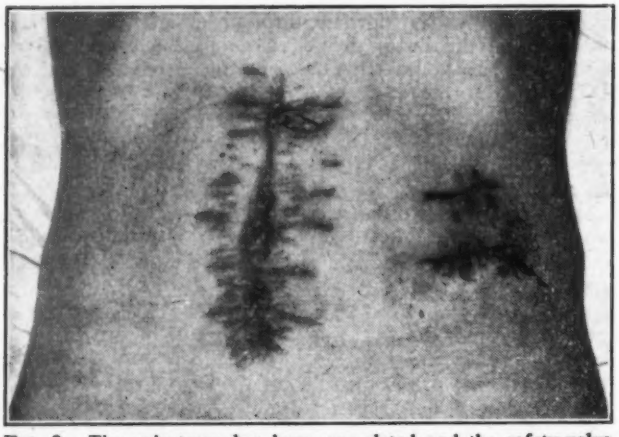

FIG. 2.—The colectomy has been completed and the safety-valve colostomy closed. The photograph is that of a child aged 10 years.

The safety-valve colostomy discharges about the third day and ileus has never been severe enough to necessitate gastric suction. Once the bowels start to function, a day or two after the colostomy has acted, the discharge from this becomes steadily less.

The improvement in the general condition of the patient is rapid. Appetite and well-being return; fever and toxaemia disappear as quickly as after an ileostomy, and the emaciated patient puts on weight.

Case Reports

Case 1.—A woman aged 30, was admitted in November, 1951, with acute ulcerative colitis supervening upon a chronic condition of 19 years' standing. Bleeding and toxaemia were severe. In spite of all forms of treatment the condition deteriorated. Sigmoidoscopy showed appearances typical of an acute stage of the condition, with changes extending right down to the anal canal. The mucinase activity of the faeces was 400 units and the pre-operative weight was 6 st. 5 lb. (40.4 kg.). Ileo-pelvi-rectal anastomosis was carried out in February, 1952. The relief of symptoms and improvement in general condition were rapid. Colectomy was postponed until September, 1952. Before it was undertaken proctoscopy revealed a rectal mucosa that appeared normal. The ulcerative condition had completely disappeared. At the final operation the outward appearances of the distal segment of the colon and the upper rectum were seen to have changed dramatically. The sodden and inflamed bowel found at the initial operation had resolved and, with the exception of a slight thickening, appeared normal. The mucinase activity in the stool at the time of the final discharge was nil and her weight was 7 st. 11 lb. (49.4 kg.). The bowels were opened eight times in the 24 hours, and she was completely continent.

Case 2.—A man aged 46 was admitted in March, 1952, with a two-years history of ulcerative colitis. He had been in hospital elsewhere for the previous six months. Recently diffuse pyodermia of his face and neck had developed. Mucinase activity of the stool was 416 units. The bowels were opened every two hours and there was a loss of weight of about 2 st. (13.2 kg.). His pre-operative weight was 8 st. 6 lb. (53.5 kg.). In view of failure to respond to medical treatment, operation was undertaken in April. Colectomy was carried out at the time of the pelvic anastomosis. Before discharge six weeks later the mucinase activity had fallen to 83 units. By September his bowels were being opened twice in the 24 hours, the pyodermia had subsided, and there was a weight gain of 17 lb. (7.7 kg.). The patient remains well. The ulceration of the rectal mucosa has healed entirely and with the exception of some oedema the mucosa appears normal.

Case 3.—A man aged 44 was admitted in March, 1952, with a seven-years history typical of ulcerative colitis. He had been in and out of hospital on numerous occasions, and in the acute attacks the rectal discharge necessitated visits to the toilet every 20 minutes. Sigmoidoscopy revealed changes of acute ulcerative colitis involving the rectum. The present attack failed to respond to medical treatment and anastomosis was carried out in May. The colectomy was completed in June. The patient's improvement was rapid. In September his bowels were opened eight to ten times a day and he was completely continent. He had gained 7 lb. (3.2 kg.) in weight, was fit and well, and was back at work. Rectal examination revealed a mucosa that was more oedematous than normal and which tended to bleed on pressure with the end of the proctoscope. The acute inflammation, with pseudo-polyposis formation present pre-operatively, had entirely disappeared. No blood was present in the stool.

Case 4.—A girl aged 10 was admitted in March, 1952, with a two-years history of periodic diarrhoea and blood in the stools. The haemoglobin on admission was 78%. Sigmoidoscopy and barium-enema examinations showed appearances of acute ulcerative colitis. The mucinase activity of the stool was 125 units. In spite of medical treatment the child's condition deteriorated steadily and multiple transfusions were required. At one time the haemoglobin fell rapidly to 46%. Blood-stained purulent discharge from the anus was almost constant, and operation was delayed only on account of the child's age. In September it seemed apparent that without operation she would die, and the anastomosis was therefore carried out. The improvement in her condition was dramatic. Three weeks later there was severe haemorrhage from the colostomy communicating with the isolated colon, and this continued. Colectomy was therefore carried out, and since that date her improvement to normal health has been uninterrupted. The mucinase activity of the stool is nil, and the rectal mucosa appears normal. The safety-valve colostomy has since been closed. There were six bowel actions in the 24 hours.

Case 5.—A woman aged 42 was admitted in July, 1952, with a 13-years history of chronic ulcerative colitis with acute exacerbations. She had been in hospital on numerous occasions. Recently there had been a steady decline in general health, constant blood-stained stools and discharge, and loss of weight. Sigmoidoscopy revealed typical changes of the condition down to the lower rectum, and barium-enema *x*-ray examination showed the terminal ileum to be involved. Ileo-pelvi-rectal anastomosis with colectomy and removal of the terminal 2 ft. (60 cm.) of small intestine was therefore undertaken. Since operation the general improvement has been great. The patient has put on 13 lb. (5.9 kg.) in weight and is in normal good health. She is completely continent, although the bowels are opened 10 times in the 24 hours. Blood is absent from the stool, and the pseudo-polyposis visualized and demonstrated by biopsy before operation has subsided.

Comment.—In the fulminating case of ulcerative colitis associated with perforation the same sphincter preservation should be aimed at. Such cases should be especially suitable for this type of operation, as the pathological changes occurring in the lower colon and rectum are acute and likely to be completely reversible. The general technique,

however, requires modification in view of the desperate condition of the patient. It is useless to attempt suture of the perforation, as the stitches will fail to hold in the diseased bowel wall, and, in any case, further perforations are usually impending at other sites in the colon. The caecum and colon as far down as the lower third of the pelvic colon must be excised, the distal end of the latter being brought out as a colostomy. Anastomosis of the ileum to the pelvi-rectal region would add a further quarter of an hour to the operation, and as the patient is unlikely to withstand this prolongation of operative time the severed end of the ileum is brought out as an ileostomy. Restoration of continuity of the bowel is delayed until the patient has fully recovered from the initial operation.

Discussion

I cannot agree with Counsell and Goligher (1952) in accepting the possibility of malignant change in ulcerative colitis as the dominating consideration in its surgical management. When true adenomata or stricture formation are present, then there is no question of the nature of the surgery that must be undertaken, but to advocate the removal of the rectum to prevent the formation of cancer when there is no certainty of its development is, I consider, too radical advice. The five specimens concerned in this article have been searched for cancer change and none has been found. It is unlikely to exist in the residua of the large bowels which have been retained, in view of the great improvement in the patients' general condition and the subsidence of the inflammatory changes, confirmed by proctoscopy. That the disease may recur in the rectum is a possibility, but the short follow-up of the present series has shown, so far, no indication of such a relapse. Even should a proportion have a return of symptoms, the establishment of an ileostomy and the excision of the rectum and terminal colon is no great surgical feat, and it can surely be reserved for those for whom it is a necessity rather than condemn all and sundry to a permanent ileostomy.

I have remarked on the noticeably smooth post-operative recovery of these patients, and from my own experience with ileostomies I have no doubt whatsoever about which is the easier. On this ground alone the operative mortality is likely to be very much less than the considerable mortality that accompanies ileostomy, and is an added argument in its favour.

Frequency of bowel action is unavoidable, but it is a small price to pay to escape an ileostomy life. In the second patient reported in the series the caecum appeared only mildly affected with the disease, and it, instead of the small intestine, was anastomosed to the pelvi-rectal junction. This patient has only two actions a day, and that this modification can be applied in other cases with advantage is a possibility.

Summary

The preservation of the rectum and of the normal channel of evacuation is advocated in those cases of ulcerative colitis in which fibrosis, pelvi-rectal suppuration, or true adenoma formation is absent from this part of the large intestine.

A method whereby this can be carried out without a preliminary ileostomy is described. The ileum is divided and its proximal end is anastomosed to the pelvi-rectal region. The colon above the site of the anastomosis is cut across and both free ends are exteriorized. The distal colostomy opening is subsequently closed and colectomy performed.

Immediate subtotal colectomy is advocated as the operative method of choice in the fulminating case.

Cases are reported in which a return to good health has followed treatment by the methods described.

I would like to thank Dr. E. R. Cullinan, in whose charge these patients have been, for his collaboration and advice in this work; Dr. C. B. Lewis, who has been responsible for the anaesthesia in these cases; and the nursing and resident staff of the Gordon Hospital for their unfailing care and attention to the patients.

Since this paper was prepared the initial stages of the operation have been successfully carried out in four other patients. One of these now has her bowels open three times a day only.

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PHLEGMASIA CAERULEA DOLENS

BY

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Phlegmasia caerulea dolens occurs in the limbs as a result of what would appear to be complete or almost complete obstruction to the venous outflow. It is of sudden onset, and is often associated with extreme cyanosis, swelling, pain, and shock, resulting in circulatory stasis of such a degree that gangrene follows in approximately a half of all cases.

The condition is rare, but has attracted much attention, particularly in France, and has been called variously pseudo-embolic phlebitis, blue phlebitis (Grégoire, 1938), and gangrenous thrombophlebitis (de Vega and Andrés García, 1946). DeBakey and Ochsner (1949) suggested the name phlegmasia caerulea dolens, and this seems an adequately descriptive term. Since then further cases have been reported (Clain and Nussbaum, 1950; Haimovici, 1950; Veal *et al.*, 1951; Miles, 1951; Turner, 1952).

Causation

The condition may occur when the main vein of a limb is suddenly obstructed. Veal *et al.* described cases that resulted from prophylactic ligature of the inferior vena cava in iliofemoral thrombophlebitis with or without embolism, and I have seen the most alarming cyanosis and swelling after ligation of the common iliac vein for repeated embolism.

On account of repeated pulmonary embolism a man aged 63 had the common iliac vein ligated, thrombosis being present in the femoral vein. The following day he was moderately shocked and complained of severe pain in the thigh and leg. The affected leg was grossly swollen, intensely cyanosed, and much colder than its fellow, the distal pulses being hardly felt. The leg was elevated to 45 degrees and reflex heating and tolazoline hydrochloride were given; within three hours the swelling had practically disappeared and a full bounding pulsation was felt in the dorsalis pedis and posterior tibial vessels.

More usually it would seem to follow thrombophlebitis, occurring spontaneously or after operation, or in the puerperium, or as a result of pressure or invasion of a vein by neoplasm, or in association with blood disease.

A woman aged 54 was admitted to hospital with a thrombophlebitis of the right leg. She had suffered from attacks of phlebitis in the right leg during the thirty months prior to admission, and two and a half years previously had had a splenectomy, at another hospital, for a supposed Banti's syndrome. She was treated in hospital with penicillin, heparin, and dicoumarol, but, as a result of haemarthrosis and epistaxis, anticoagulants had to be stopped. Five weeks later there was a sudden onset of severe pain, swelling, and cyanosis of the right leg.

On examination the patient was seen to be severely shocked, the right leg was intensely swollen and cyanotic up to the knee, and the distal half of the leg was cold and pulseless. The femoral pulse was palpable, but more distal pulses were not felt. A diagnosis of embolus was considered, but no origin was apparent, and it was thought that the ischaemia was the result of a massive venous obstruction.

Conservative treatment by elevation, reflex heating, and tolazoline hydrochloride was instituted, but after three days it was obvious that a patch of tissue in the sole of the foot was gangrenous. The swelling gradually subsided and the cyanosis diminished slightly. Investigation of the blood showed a polycythaemia vera, which was treated by radioactive phosphorus. After five weeks the gangrenous area, fortunately small and superficial in extent, sloughed and distal pulses became palpable. However, cyanosis and moderate swelling persisted and it became evident that all the superficial veins of the limb were thrombosed, and that there was a thrombosis of the inferior vena cava.

Six months later the patient was getting about, with the legs bandaged to control the swelling, and the pulses were all normal, a foot plethysmograph at this time showing a greatly diminished but adequate flow in the right foot with no response to reflex heating, thus indicating venous obstruction of such a degree that no reserve blood flow was available.

Massive venous thrombosis as a result of polycythaemia vera in this case caused such a degree of venous obstruction as to jeopardize the life of the limb. Swartley *et al.* (1942) reported a case occurring in an upper extremity, resulting in gangrene of the forearm.

Why only a minute proportion of cases of thrombophlebitis are followed by this train of alarming symptoms is not at present understood, and there are certainly other factors concerned apart from venous obstruction from thrombophlebitis.

Clinical Features

Clinically, the onset is one of dramatic suddenness and is associated with severe pain, sometimes of the greatest intensity. At the same time there is marked swelling of the limb, associated with shock which may even be fatal, and cyanosis occurs which varies greatly in degree, but which may be almost black. The arterial pulse may not be detectable in the distal parts, and the swelling of the limb will render its detection even more difficult. The limb rapidly cools off, and the appearances are similar to those of arterial embolism; this has led to exploration of the femoral artery on a number of occasions (Audier, 1935; Wertheimer and Frieh, 1935; Lindgren, 1937; and Sackenreiter, 1940). Gangrene may ensue, and may be of any degree from a superficial necrosis to a massive death of tissue demanding major amputation which is fatal in 25% of cases. On the other hand, the condition may settle down slowly, the swelling and cyanosis gradually disappearing, and the limb circulation returning almost to normal with or without a post-phlebitic syndrome of varying degree persisting. Sometimes recovery is as sudden as the onset, and it may be partial or complete. Death may occur at the onset from shock associated with loss of fluid into the affected limb and excessive pain, or it may occur later on as a result of gangrene. Pulmonary embolism is a common complication. There seem to be two main varieties, either swelling and cyanosis or arterial symptoms predominating, the latter simulating embolism. More often the types are mixed and there are signs of both venous and arterial occlusion.

It has been shown experimentally (Audier and Haimovici, 1938) that gangrene due to venous obstruction in an organ can be produced only if every vein draining that organ is ligated—in other words, if there is complete venous obstruction—and it may be that in some cases which proceed to massive gangrene this is in fact the mechanism. If this were so, recovery would seem impossible and recanalization could not occur in time to prevent massive death of tissue.

Illustrative Cases

As in fact most cases recover to a greater or less degree—sometimes with no loss of tissue, sometimes with minor gangrene—it seems to me that factors other than total venous obstruction must be significant in this syndrome.

A man aged 67 developed, on the fourth day after a partial gastrectomy, a sudden intense swelling of the left lower extremity up to the level of the groin, and the swollen limb became deeply cyanotic. He was severely shocked, and examination showed a palpable femoral pulse but no distal pulses, and the whole limb was much cooler than the unaffected limb. The next day, after a sudden pain in the chest, the patient died. Post-mortem examination revealed a pulmonary embolus as the immediate cause of death, and the affected limb showed a recent acute thrombophlebitis of the internal saphenous vein, the result of an infusion into this vessel, with no evidence of thrombosis of any other vein, and with no obstruction to the arterial tree.

In this case it seems that an acute superficial thrombophlebitis may have induced a spasm in either the veins or the arteries, or in both the veins and the arteries, of the limb, resulting in cessation of the circulation.

De Sousa Pereira (1946) found that where an isolated segment of vein is the site of thrombophlebitis there is accompanying venospasm extending far beyond the vein affected, and that this spasm can be relieved by anaesthesia of the vein wall or by interruption of the efferent pathways of the sympathetic chain. That veins can go into very effective spasm will be agreed by anyone who has had the experience of intravenous therapy or of operations on veins. Even varicose veins, where muscular walls are atrophied and often largely replaced by fibrous tissue, may be seen to contract.

Diminished oscillations of an artery in close proximity to a vein which is the site of thrombophlebitis has been demonstrated by DeBakey *et al.* (1939), and the association of arterial spasm with deep thrombophlebitis has been emphasized by Boyd (1947). Sutton (1952) reported a case of spasm of the brachial artery of such a degree as to render the hand and fingers bloodless after an intravenous infusion into the superficial median basilic vein at the elbow.

A woman aged 25, thirty weeks pregnant, was admitted to hospital complaining of a cramp-like pain in the left leg on movement. On lying in bed there was a dull ache in the limb together with a feeling of numbness. The limb was pulseless from the femoral artery downwards, there was a patchy cyanosis, and both leg and foot were cold. Sensation was normal and the toes could be moved voluntarily. The picture suggested an embolus, but there was no apparent origin for this, and the case was treated conservatively. Among other procedures, heparin was given via intravenous saline drip. On the third day, while I was examining the patient, she had a rigor, and the most remarkable change came over the affected limb, the cyanosis being replaced quite rapidly by an intense hyperaemia, the pulses throughout the limb becoming full and bounding, and the temperature of the limb gradually becoming higher than its contralateral fellow. Two weeks later the only abnormality was a mild post-phlebitic syndrome.

It seems that in this case an idiopathic deep thrombophlebitis initiated a severe degree of arterial spasm. No doubt sudden rigor was the result of impurities in the heparin and saline drip, and gave rise to a functional sympathectomy which itself "released" the spasm. Dissection of amputated limbs and post-mortem specimens has shown an apparently healthy arterial tree without any evidence of obstruction, though limbs removed by delayed amputation may show the distal arteries close to the gangrenous area filled with thrombus.

Discussion

In phlegmasia caerulea dolens the disappearance of the arterial pulse may be due to a reflex arterial spasm initiated by an irritative thrombophlebitis. On the other hand, when there is oedema and swelling of an extremity resulting from venous obstruction the digital pulse may become impalpable. In fact, in such a limb oscillations recorded by a sensitive galvanometer may be completely masked in spite of a normal blood flow. Clinically, therefore, disappearance of the distal pulses may not necessarily indicate any active spasm of the arteries, especially in those cases in which the swollen cyanotic type of affection predominates. There is no doubt that massive thrombosis of all, or the vast majority, of the veins of the limb results in gangrene, but in those cases in which recovery takes place partial venous obstruction by

thrombus is rendered temporarily complete by an associated spasm of the remaining veins in the limb. At the same time there may be some degree of arterial spasm as well, and it is these several factors, varying in degree, which give rise to the different clinical varieties.

The condition may well be of medico-legal importance, for the development of gangrene in a limb following operation for varicose veins does not necessarily mean that the main artery or even the main vein has been tied.

Much of the treatment is indicated by the pathology. Heparin should be given to achieve and maintain a clotting-time of 15 to 20 minutes, and associated shock is treated by transfusion and other methods. The affected limb should be elevated to an angle of at least 45 degrees to take the best advantage of gravity, and, if the patient's general condition allows, supervised active exercises should be vigorously pursued.

Veal *et al.* recommended this treatment in all cases, and considered that any sympathetic release should be avoided, as it increases the embarrassment of an obstructed venous system. They also stated that if the condition follows ligation of a main vein the ligature should be removed immediately.

If, however, the argument is accepted that the obstruction to the venous drainage is to some degree functional, then it would appear advisable to try to break this reflex by a method of sympathetic release, and, as I have indicated above, it seems to me that there must be a large measure of spasm, at least in those cases which have a chance of recovery.

In a heparinized patient any sympathectomy by resection or by paravertebral injection is dangerous and very likely to produce a retroperitoneal haematoma, and should therefore be avoided. A quite adequate sympathectomy can readily be achieved by means of heat applied to the trunk and unaffected limbs, liberal doses of alcohol, one of the best available vasodilators, and the induction of deep sleep with soluble amylobarbitone in doses of 3 gr. (0.2 g.) hourly until the patient is difficult to rouse, or liberal doses of morphine if pain is severe. This is a regimen appreciated by patients, and it has the advantage of allaying anxiety, besides achieving its effect on the sympathetic. The affected limb should be kept at room temperature, as should any limb threatened with gangrene, and intra-arterial tolazoline may be tried, although I have not been very greatly impressed with this procedure, and my own preference is for the intravenous route in urgent cases. As soon as the patient is fit enough, the elevated limb should be exercised actively several times a day under the supervision of a physiotherapist. In many cases the swelling resolves, the pain is relieved, and the circulation returns, often rather suddenly, in whole or in part. If return of circulation is incomplete, massive or superficial gangrene may result. Pulmonary embolism is a common danger, but heparinization will tend to prevent this complication. In the event of minor or major gangrene developing, removal of tissue (or amputation) should be restricted to the dead part, since the circulation in the surviving proximal segment has always completely recovered before the need for ablation of dead tissue arises.

Summary

The association of acute ischaemia or even gangrene with thrombophlebitis of the extremities is discussed, and the name phlegmasia caerulea dolens is considered to be adequately descriptive.

The different clinical manifestations are described.

The mechanism of the ischaemia is considered, and a theory advanced to account for the varieties.

Treatment is described in outline.

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SURVIVAL OF TRANSFUSED RED CELLS IN SCURVY

BY

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The pathogenesis of the anaemia of scurvy is obscure. One view is that the mechanism may be inadequate haemopoiesis due to deficiency of vitamin C. Vilter *et al.* (1946) and others have suggested that there may be a haemolytic process.

The theory of haemolysis has been based on the occurrence of reticulocytosis and abnormally high serum bilirubin and faecal and urinary urobilinogen values in patients with scurvy and anaemia. These findings are not necessarily due to haemolysis. A more reliable indication may be obtained by studying the fate of transfused red cells. As search of the literature has not revealed any report of such an investigation in scorbutic patients, studies of the survival of transfused cells have been made in eight patients with scurvy and anaemia and in one with scurvy but without anaemia.

In six of these patients the transfused red-cell survival time was greatly reduced, and this was interpreted as evidence of a haemolytic process.

Material and Methods

Eight adult male patients (seven Bantu and one Indian) who manifested severe scurvy and anaemia with normoblastic bone marrow have been investigated. The ninth patient, an adult male Bantu, was scorbutic but not anaemic. For some time before admission to the Groote Schuur Hospital these patients had been on a diet severely deficient in vitamin-C content, consisting almost solely of mealie meal (maize) and white bread. All presented the classical picture of scurvy, with spongy haemorrhagic gums, follicular hyperkeratoses, and intramuscular haematomata. There were no signs of any other disease.

The investigation of the eight anaemic cases was divided into four stages as follows:

(1) Initially the patient was kept at complete rest in bed, without any medication and on a diet entirely lacking vitamin C (mealie meal porridge without milk or sugar, stamped mealies, white bread without butter or jam, and black tea and coffee).

(2) After the short control period of rest in bed, the patient was given one transfusion of citrated bank blood which had been stored for at least 36 hours. Between 2 and 4 pints (1.1 and 2.3 litres) of blood were given in each case according to the degree of anaemia. The vitamin-C content of the blood used in each transfusion was not determined, but the average vitamin-C content of 8 pints (4.5 litres) of blood, taken and stored for 36 hours under the same conditions

as the transfused blood, was found to be 1.45 mg. per 100 ml. The vitamin-C-free diet was maintained during this stage.

(3) Between 8 and 18 days after transfusion the patient was given by intramuscular injection 500–1,000 mg. of ascorbic acid daily for a period of 6–10 days while still receiving the vitamin-C-free diet.

(4) Finally, the patient was given a full diet.

In Case 5 the investigation had to be curtailed because he developed chest pain, possibly due to pulmonary embolism. He was therefore given vitamin C on the third post-transfusion day.

In the non-anaemic patient a blood transfusion was given on the day of admission to hospital without a preliminary period of observation. He was investigated for six days thereafter whilst kept in bed on the vitamin-C-free diet without any other medication. On the seventh day he demanded his discharge. He was given 1,000 mg. of ascorbic acid intramuscularly and a full diet; he was subsequently seen as an out-patient.

The red-cell survival times were determined by the Ashby technique, using potent anti-A and anti-B sera (Mollison, 1951). In Case 6, with blood group O, powdered anti-M serum in the form of powdered globulin was used. The estimations of survival times were made either daily or on alternate days. In Cases 2 and 3 the estimations were made on capillary blood. In the other seven cases venous blood was used. In each estimation at least 2,000 cells were counted.

Whilst the patients were on the control diet every possible precaution was taken to prevent them from receiving extraneous sources of vitamin C, apart from the ascorbic acid given by injection and the small quantity in the transfused blood. In error Case 6 was given a glass of sour milk on the sixth day after transfusion, but no other breach of the strict dietary control is known to have occurred.

No other medication was given at any stage except that Case 4 received one injection of 25 mg. of A.C.T.H. on the 18th day after transfusion for the purpose of testing adrenocortical function. This patient bled severely on that day and was immediately given a second blood transfusion; in all other cases only one transfusion was given. As part of another investigation four cases (Nos. 2, 5, 7, and 9) received an intravenous injection of the sodium salt of *para*-aminohippurate; in addition Cases 2 and 5 received an injection of sodium thiosulphate, whereas Cases 7 and 9 were given inulin.

Results

The Table shows blood findings in each patient before and after transfusion, before vitamin-C therapy, and on discharge. Figs. 1 and 2 show the red-cell survival times for the nine cases.

In Cases 2, 5, and 8 the red-cell survival could not be regarded as being abnormal. In Case 2 the survival-time curve was normal except that the red cells seemed to disappear rapidly at a stage one week after the beginning of vitamin-C therapy. Cases 5 and 8 were followed for only three and six days respectively before being given vitamin C.

In the remaining six cases (Nos. 1, 3, 4, 6, 7, and 9) the transfused red-cell survival times were much shortened. The effect of administering vitamin C in these six cases was as follows. In Cases 3, 6, and 7 the abnormal degree of red-cell destruction diminished coincidentally with the administration of ascorbic acid as indicated by the flattening of the red-cell survival curves. In Cases 1 and 9 the increased rate of destruction persisted for two to three days after ascorbic acid therapy was started. Case 4 was investigated for 18 days before ascorbic acid was given. On the 18th day he bled severely from nose, mouth, and gums, and required a second blood transfusion. An injection of 25 mg. of A.C.T.H. had been given on that day to assess adrenocortical function. The increased rate of disappear-

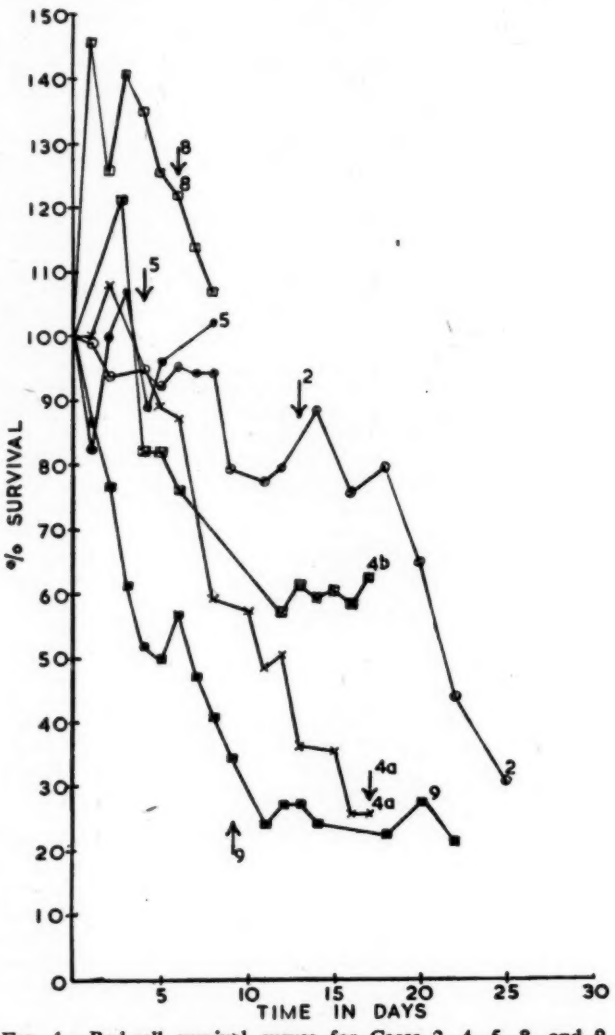

FIG. 1.—Red-cell survival curves for Cases 2, 4, 5, 8, and 9. Case 4 received two transfusions. The arrow indicates the beginning of treatment with ascorbic acid.

Blood Findings

	Case 1		Case 2		Case 3		Case 4, *a*		Case 4, *b*		Case 5		Case 6		Case 7		Case 8		Case 9	
	Hb %	Transfused Cells %	Hb %	Transfused Cells %	Hb %	Transfused Cells %	Hb %	Transfused Cells %	Hb %	Transfused Cells %	Hb %	Transfused Cells %	Hb %	Transfused Cells %	Hb %	Transfused Cells %	Hb %	Transfused Cells %	Hb %	Transfused Cells %
Before transfusion ..	54	0	38	0	80	0	72	0	41	24	51	0	51	0	22	0	90	0	30	0
After ..	64	100	66	100	97	100	68	100	73	100	76	100	91	100	56	100	105	100	53	100
Before vit. C ..	63	49	89	80	104	44	41	24	—	—	79	89	58	60	39	54	100	122	43	41
Last observation ..	89	37	96	30	98	36	—	—	95	62	85	102	88	35	67	38	100	107	82	21
Day vit. C started ..	10		13		13		18		0 (18)		3		10		10		6		8	
Day of last observation	28		25		22		—		25 (44)		8		30		34		12		22	

ance of the donor cells continued after haemorrhage ceased, and the red-cell survival curve did not flatten until 9–10 days after the beginning of ascorbic acid therapy.

Haemoglobin values were determined in each case *pari passu* with the estimation of volume of packed red cells.

Of the six cases in which there was rapid disappearance of donor cells, four (Cases 4, 6, 7, and 9) showed a fall of haemoglobin simultaneously with the decrease in volume of packed red cells, whilst in Cases 1 and 3 the haemoglobin did not drop below the immediate post-transfusion level. It is noteworthy that in Cases 4 and 9 the fall of haemoglobin and packed cell volume occurred despite a great increase of reticulocytes.

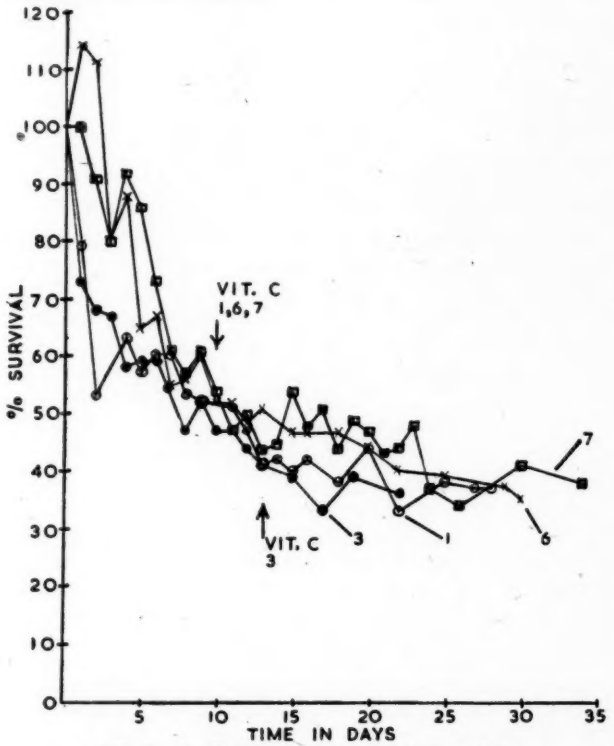

FIG. 2.—As for Fig. 1. Cases 1, 3, 6, and 7.

Of the three cases (Nos. 2, 5, and 8) in which the red-cell-survival times were found to be normal, the one which could be followed adequately (Case 2) had haemoglobin above the post-transfusion level. In this patient there was a marked reticulocytosis on the day of transfusion and for several days thereafter. This could be attributed perhaps to rest in bed or possibly to some intake of vitamin C a few days previously of which no history could be obtained. The degree of anaemia in Cases 2 and 5 before transfusion was as severe as that of patients in whom the red-cell survival was very much reduced.

All the patients were Rh-positive. The direct and indirect Coombs tests were negative in every case. All recovered completely and were discharged from hospital feeling well.

Comment

It appears that at least in some cases of scurvy with anaemia there is an abnormally rapid rate of disappearance of transfused red cells.

The phenomenon of excessive rate of disappearance of donor cells may be due to either haemorrhage or haemolysis. In the six cases described above in which transfused red cells disappeared rapidly there was no haemorrhage to account for this. The gums were haemorrhagic, but the loss of blood from this source is negligible, as the tests for occult blood in the stools were almost invariably negative. In Case 4 there was considerable haemorrhage, but the disappearance of donor cells had been excessive prior to this, and continued to be excessive even after haemorrhage ceased. The patients had intramuscular haematomata, but these did not seem to increase in size after transfusion. This is not a matter on which one can dogmatize, since the haematomata were not measured. The shortened survival time of red cells seemed to be due to haemolysis.

Pigment studies, such as the measurement of stool and urine urobilinogen excretion, were not made in these patients. Bronte Stewart (1950, 1953) studied a similar group of patients with scurvy and anaemia in this hospital who were not transfused. He found that their urobilinogen excretion was greatly increased above normal values. This was related in large degree to the presence of intramuscular haematomata. He was unable to interpret his findings as providing positive evidence of an intravascular haemolytic process, although the occurrence of such haemolysis could not be excluded with certainty.

The course of the anaemia of scurvy patients who are merely put to rest in bed, without any other therapy and while still receiving a vitamin-C-deficient or vitamin-C-free diet, is important in this discussion. Other workers have reported observations on this point. In a few cases there has been spontaneous remission of the anaemia (Ungley, 1938; McMillan and Inglis, 1944; Vilter *et al.*, 1946). In the majority the anaemia has remained stationary (Mettier *et al.*, 1930; Ralli and Sherry, 1941; McMillan and Inglis, 1944; Vilter *et al.*, 1946).

In occasional cases there has been a rapid increase in the degree of anaemia despite increased reticulocytosis (Mettier *et al.*, 1930; Jennings and Glazebrook, 1938; Vilter *et al.*, 1946; Bronte Stewart, 1950; Brown, 1951).

It is not clear why there is this variability of course of the anaemia on rest in bed alone. Pirani (1952) has shown that small but significant amounts of ascorbic acid are present in the adrenal glands and other tissues even in the most advanced states of scurvy. It is possible that rest in bed might promote remission of the anaemia by diminishing the general metabolic demand for vitamin C and thereby making the tissue vitamin-C reserves available for erythropoiesis. Whether or not this will occur might depend on the ratio of the amount of vitamin C available to the amount required.

Such a balance mechanism might account for the extremely rapid disappearance of donor red cells in so many cases in this investigation, because the large transfusion of blood increases the general metabolic demand for the inadequate amount of available tissue vitamin C.

The speed with which donor cells were eliminated and the rapid fall in the patients' haemoglobin appeared to be in excess of the fall in haemoglobin observed by other authors in patients who had not been transfused and who had been kept in bed on a vitamin-C-free diet.

Thus, whilst the results of this investigation support the view that there is a haemolytic factor causing diminished survival time of red cells transfused to scurvy patients, they do not necessarily indicate that a haemolytic process is the cause of the anaemia in untreated cases. Further investigation to elucidate this point is planned.

It is curious that the abnormally rapid rate of red-cell destruction appeared to persist in three cases for some days after vitamin-C therapy was begun. It is possible that the cells were "prepared for destruction" and could not be saved by the treatment. Alternatively, it is possible that the haemolytic mechanism persisted for some days owing to some tissues having a prior claim to the added vitamin C.

Summary and Conclusions

Eight cases of scurvy with anaemia and one without anaemia have been observed whilst at rest in bed on a vitamin-C-free diet. Transfused red-cell survival times were determined in each case and found to be abnormally short in six of the nine patients. In three of these six patients the increased rate of red-cell destruction

persisted for some days after the beginning of vitamin-C administration. In the remaining three of the nine patients the donor red-cell survival times appeared to be normal, but two of these cases could not be studied adequately, and even the one who was adequately followed showed a rapid fall in the number of transfused red cells one week after vitamin-C therapy was started. It is possible that the blood transfusion materially increased metabolic demands for vitamin C, and this factor may have contributed to the rapid destruction of donor cells. With this reservation, the results of this investigation support the view that a haemolytic process is an important factor in the pathogenesis of the anaemia of scurvy.

ADDENDUM.—Since this paper was prepared an additional nine Bantu male patients with scurvy and normoblastic bone marrow have been studied by the same methods. Three of these, who were severely anaemic, were transfused with sedimented red cells from 1 pint of blood. All three patients eliminated the transfused red cells very rapidly. In the remaining six patients 1 pint of blood was first removed; subsequently they were transfused with 1 pint of blood. Red-cell survival was greatly decreased in five of these patients, the sixth patient having a normal red-cell survival time. The sixth patient (and one of the five with diminished red-cell survival) was not anaemic. The other four were anaemic. It appears that the proviso inserted in the main body of the paper that overtransfusion might be playing some part in the abnormal red-cell survival in untreated scurvy is unnecessary. Red-cell survival was abnormal even when a replacement transfusion was substituted for simple transfusion. An increase in the protein content of the diet by the addition of thoroughly stewed meat also did not alter the diminished red-cell survival in the last four patients studied. In the combined series there were thus 14 anaemic patients and 2 non-anaemic patients who were maintained on the vitamin-C-free diet for more than seven days. Of the anaemic cases 13 had greatly diminished red-cell survival. Of the non-anaemic cases, red-cell survival was normal in one and diminished in the other.

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The Association of Universities of the British Commonwealth has published a useful list of postgraduate fellowships, scholarships, grants, etc., for advanced study and research, tenable at universities in the United Kingdom, together with details of some of the more important awards tenable overseas by British graduates. The list is published by the Association at 5, Gordon Square, London, W.C.1. Academic interchange between the universities of Britain and those of other European countries has been sponsored by the British Council for several years. The Council has now published a pamphlet (*University Interchange between the United Kingdom and other European Countries, 1948–1953*) listing all such interchanges.

CEREBELLAR NECROSIS IN A CASE OF SUBARACHNOID HAEMORRHAGE

BY

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The possible dangers from lumbar puncture to patients with increased intracranial tension are well known. The main one is forcible impaction—"coning"—of the brain-stem and cerebellum into the foramen magnum, following excessive and rapid drainage of cerebrospinal fluid from the lumbar theca. This may or may not be accompanied by uncal herniation through the tentorium cerebelli. These risks are mentioned only briefly in the standard neurological textbooks, but their mechanisms have received some close attention in the literature (Jefferson, 1938; Cairns, 1939).

A less frequently cited complication is the precipitation of cerebral haemorrhage, and Schube and Raskin (1936) mention 14 examples occurring in the literature. Two of these were cases of cerebral aneurysm. Androp (1939) reports a case in which death occurred, following lumbar puncture, from haemorrhage into the spinal cord and brain-stem.

Necrosis of the cerebellar tonsils was present in the following case of subarachnoid haemorrhage due to rupture of a cerebral aneurysm. Lumbar puncture was performed three times in the course of the illness. This necrotic lesion is considered to have resulted from an extreme and possibly prolonged degree of coning of the cerebellum. So far as I am aware, such a lesion has not been described before.

Case History

A 41-year-old housewife was admitted in an unconscious state to a country hospital in Northern Ireland on November 14, 1951. She had complained of headache since November 9, and had collapsed on the 13th. On examination there was pronounced neck stiffness, and a subhyaloid haemorrhage was present below the right optic disk. At lumbar puncture the fluid was blood-stained and under obviously greatly increased pressure. The supernatant fluid was xanthochromic.

The patient's condition improved somewhat until November 17; she was more conscious, but now complained of diplopia, although an external ocular paresis could not be demonstrated. On the 19th lumbar puncture was repeated, and yellow fluid not under increased pressure was obtained. Following this, she complained of headache, and became drowsy. A right lower facial weakness was noticed at this time.

Again there was some improvement, and on November 24 lumbar puncture was performed for the third time. A few drops of clear fluid, not under pressure, were obtained. In a matter of minutes she became shocked and lapsed into semicoma.

The patient was transferred to the neurosurgical unit at the Royal Victoria Hospital, Belfast, where she arrived at midnight of the same day. She was deeply comatose on admission, with marked neck stiffness, extensor plantar reflexes, and B.P. 150/80 mm. Hg. The pupils were unequal, and fixed in dilatation. Papilloedema was not thought to be present. *X*-ray examination of the skull failed to reveal any fracture, and the pineal gland was not visible.

Operation was undertaken immediately. In view of the previous right-sided signs, a left temporal burr-hole was made under local analgesia. The dura was found to be

tense, but needling did not produce any fluid, bloody or otherwise. Three burr-holes were then made on the right side, and dark blood clot and old blood were evacuated from both the subdural and the subarachnoid spaces on that side. A pronounced but only transient improvement took place in the patient's condition, and death occurred at 5 p.m. on November 25.

Post-mortem Findings.—Necropsy was performed 17½ hours after death. On opening the skull an extensive subarachnoid haemorrhage became apparent, and it was found to be present chiefly over the base of the brain, more particularly on the right side. Its source was a ruptured aneurysm 1 cm. in diameter on a branch of the right middle cerebral artery, fairly high in the Sylvian fissure. The brain was generally swollen, the right temporal lobe more than the left. On sectioning the brain the subarachnoid haemorrhage was seen to extend for about 3 cm. into the substance of the right temporal lobe from the region of the aneurysm. No other intracerebral haemorrhages were revealed. Gross hernias of the unci and cerebellum were observed, the latter very marked indeed, so that it was only with difficulty that the cerebellar tonsils and the brain-stem could be delivered from the foramen magnum. The lower 1.5 cm. of the tonsils was swollen, discoloured, and haemorrhagic. Histological sections from these affected areas showed recent haemorrhagic necrosis, in which there was an acute inflammatory cell reaction, together with fibrinoid necrosis of the walls of several small vessels.

Discussion

The clinical diagnosis of subarachnoid haemorrhage, including episodes of unconsciousness, could be satisfactorily, if superficially, confirmed at necropsy on the basis of the findings described above. It is in trying to reconstruct the precise chronological details of these changes that problems arise.

It is probable that a potentially reversible degree of uncomplicated cerebellar coning developed early in the clinical course. However, the age of the necrotic process in the tonsils was only about 24–48 hours. This particular lesion, if precipitated by lumbar puncture, was more likely to be related to the last occasion than to the first two. The intracerebral haemorrhage, too, was of recent occurrence, but its histological details do not permit of such an accurate estimate of its age. It may have been precipitated also by the third lumbar puncture, but equally well may have arisen earlier, either spontaneously or in relation to the previous lumbar punctures. Irrespective of when and how this latter haemorrhagic lesion took place, it seems indisputable that it materially aggravated the degree of cerebellar coning already present. Schaller (1933) and Masserman (1934) pointed out that foraminal herniation is due not so much to a direct "plugging" effect following the withdrawal of cerebrospinal fluid as to oedema of the brain which develops subsequently. An intracerebral haemorrhage could be visualized easily as contributing to this. Clearly, in the present case, at least three distinct factors—subarachnoid haemorrhage, cerebral haemorrhage, and lumbar puncture—interacted in a complex manner to produce the pathological end-result described.

These speculations, academic and inconclusive though they may be, do not invalidate the general warning of the dangers of injudicious lumbar puncture in cases of subarachnoid haemorrhage. It is impossible to escape the conclusion that lumbar puncture in this case contributed at least to the cerebellar coning and necrosis, and possibly further subarachnoid bleeding. It would seem that, once the diagnosis is established by the withdrawal of evenly blood-stained fluid which leaves a xanthochromic supernatant fluid after centrifuging, there are no further indications for lumbar puncture in cases of subarachnoid haemorrhage.

Summary

A case of subarachnoid haemorrhage due to rupture of a cerebral aneurysm is described. Death occurred after the third lumbar puncture. At necropsy, cerebral haemorrhage, cerebellar coning, and tonsillar necrosis were found. No reports of the last-named lesion can be found.

I am grateful to Professor J. H. Biggart and Dr. J. E. Morison for assistance and criticism. Mr. C. A. Calvert, F.R.C.S., kindly gave me permission to publish this case.

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ACUTE DERMATOMYOSITIS

BY

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Recent articles (Oppel *et al.*, 1950; Thorn *et al.*, 1950; Suzzman and Rudolph, 1951) have shown the value of cortisone and A.C.T.H. in acute dermatomyositis. A further case of this rare disease responding dramatically to cortisone therapy is described.

Case History

A domestic servant aged 24 was admitted to the Central Middlesex Hospital on May 14, 1952. She had been in good health till three months previously, when her fingers became stiff and swollen at times. A week before admission her left hand felt weak, and the following night a sensation of tightness developed in her throat. She could not swallow properly. When she awoke the following morning (May 10), both hands felt weak. They were not painful. The weakness and stiffness of the finger- and wrist-joints soon involved the elbows and shoulders, and later both her knees and hip-joints and her back. Her legs felt useless and her muscles became increasingly painful and tender to pressure. On the same day a bright red rash started on the dorsal surface of her hands, soon spreading up both arms, and a similar rash involved both legs. On May 12 her eyelids felt swollen and stiff and they were red-rimmed. This condition lasted only a few hours. Throughout this time she felt ill and had lost her appetite completely. She vomited on three occasions. Each movement was an effort, and she ached all over when she attempted to shift herself in bed.

Physical examination showed her to be well nourished but very ill. Her temperature was 104.6° F. (40.3° C.). Her tongue was heavily furred, and her skin was hot and clammy. There was a diffuse confluent erythematous rash on the dorsal aspects of both feet and on the upper arms. In other areas irregular red macules were present. The rash was mainly confined to the limbs, but had a few extensions on the skin of the abdomen and back. She was profoundly weak, being unable to sit up, and only with difficulty could she straighten her arms or bend her knees. All her muscles were tender on palpation and felt firm and full. The superficial reflexes were normal.

On May 15 her temperature was 103° F. (39.4° C.). The rash appeared to be clearing from the forearms and from the dorsal surfaces of her feet. However, she seemed weaker and to have become worse. She was totally unable to move herself and could swallow fluids only, as she had marked dysphagia. She had a troublesome watery diarrhoea and retention of urine developed, which required catheterization. Her general condition was deteriorating so rapidly that it was decided to give cortisone immediately, and 100 mg. was injected intramuscularly at 5.30 p.m. An hour later she could move herself in bed more freely and could bend her

knees. Next morning there was definite improvement. The temperature had fallen to 101.8° F. (38.8° C.). She could raise her arms above her head, sit up without help, and swallow without difficulty. Her muscles felt flabby and hypotonic. The knee-jerks had returned. The rash was fainter. Cortisone, 100 mg. twice daily, was given.

Improvement continued, and within four days the temperature had fallen to 98.6° F. (37° C.), the rash had almost completely faded, and her general condition had improved so greatly that cortisone was discontinued. The following day she had a partial relapse. The muscles became more tender and tense and she had two rigors, the temperature reaching 102° F. (38.9° C.). Cortisone, 25 mg. six-hourly, was recommenced.

On May 21 the rash reappeared on the back of both hands and the front of both arms. It was bright red and confluent. Her limb movements, however, were now quite free and her muscles were not tender. The rash became more extensive for the next two days. On the elbows and knees it was confluent, the flexures were pinky red and the eyes were red-rimmed. It then began to fade once more, and was last seen on May 6, when only small erythematous areas on the left forearm were noted.

On June 3 cortisone was discontinued. A.C.T.H. gel, 40 I.U. twice daily intramuscularly, was begun. For two days after the change there was a recurrence of slight muscle stiffness, and on June 5 the temperature rose to 102.4° F. (39.1° C.). However, the patient became rapidly stabilized on the dosage, and on June 10 she was allowed up.

On June 17 the A.C.T.H. dosage was reduced to 40 mg. once daily, and ten days later it was discontinued altogether, the patient having then had 1,500 mg. of A.C.T.H. and 2,200 mg. of cortisone in 43 days. Her history was now one of gradual but continued improvement. Muscle power increased steadily. At first inclined to shuffle along and to tire easily on walking, she walked normally on discharge. She could write distinctly and effortlessly. On July 8 she was discharged. There were then no abnormalities on physical examination.

The patient returned to her home in Ireland two days after discharge from hospital and has written to me on several occasions since. She has remained well, but complained of some weakness and stiffness of her wrist and finger-joints about six months after her return. As this continued she was admitted in April, 1953, at my request, to St. Laurence's Hospital, Dublin, under care of Dr. H. J. Counihan, who wrote to me that the changes present were like those of rheumatoid arthritis and that, apart from these changes in her fingers, her general condition was satisfactory. She was discharged from hospital again in May, 1953, and has been receiving injections of cortisone. According to the patient, her fingers and wrists have become fully mobile again—so much so that she is returning to London to recommence work shortly.

Most of the significant investigations are summarized in Table I.

TABLE I.—*Blood and Urine Investigations in Case of Dermatomyositis*

Date	Hb %	Leucocyte Count	Seg. Polys. (%)	Staff Cells (%)	Juvenile Polys (%)	Myelocytes %	Eosinophils %	Lymphs %	Monos %	Creatine Excretion (mg./24 hrs.)	E.S.R. mm./hr. Westergren
14/5/52		9,600	90	1	—	—	4	5	—	—	33
15/5/52	Cortisone begun										
16/5/52										710	
18/5/52										376	
21/5/52	69	59,800	55	34·5	2·5	3·5	—	4	0·5	40	23
27/5/52											11
30/5/52		13,000	82	5	—	—	—	13	—		
3/6/52											21
10/6/52											11
11/6/52										7·3	
24/6/52											7
27/6/52	Hormones (A.C.T.H.) discontinued										
8/7/52	90	5,300	71	2	2	—	—	22	3		4

A muscle biopsy was carried out, and Dr. Walter Pagel reported as follows: "Fragments examined are fat tissue with some haemorrhages and peripheral muscle, with some occasional hyalinization, but without any regenerative or inflammatory cellular changes. The nuclei are well stained throughout." It is possible, however, to obtain an indefinite or negative biopsy report on material obtained from one muscle while material from another shows typical changes (W. Pagel, 1952, personal communication). Suzzman and Rudolph's case also lacked a positive biopsy report, but was in every way a typical acute example of the disease.

Not much emphasis has been laid on the quite frequent occurrence of a polymorphonuclear leucocytosis in acute dermatomyositis, but cases besides the present one showing this feature have been described (Table II).

TABLE II.—*High Leucocyte Counts Found During Course of Acute Dermatomyositis*

	White-cell Count	Polymorpho-nuclears	Primitive Polymorphs
Keil (1940)	70,000	With polymorphonuclear leucocytosis	
Holmes (1948)	63,600	89%	
Oppel *et al.* (1950) ..	64,600	60%	34%
Suzzman and Rudolph (1951)	31,000	81%	5%
Clein (1953)	59,800	55%	40·5%

Summary

A case of acute dermatomyositis in a young woman is described, the diagnosis being made on the classical clinical picture presented, despite the absence of definite histological proof. Prompt remission following the use of cortisone was noted, with partial relapse when it was discontinued too soon.

Emphasis is laid on a high polymorphonuclear leucocyte count during the course of the disease.

Treatment with A.C.T.H. or cortisone is believed to be the method of choice in acute cases.

I should like to thank Dr. R. A. J. Asher for his encouragement and permission to report this case, which was treated under his care; Dr. W. Pagel for carrying out the pathological examination and for advice; Dr. D. A. Brewerton for many helpful suggestions; and Dr. H. J. Counihan for reinvestigating the patient and forwarding his helpful report to me.

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The Wellcome Film Unit has produced two new 16 mm. films entitled "The Dissection of a Mosquito for Malaria Parasites" and "Pinning Mosquitoes," both in colour with sound. The first is a demonstration by Mr. P. G. Shute of the Medical Research Council's Malaria Reference Laboratory. After showing the phases of the life cycle of the malaria parasite within the mosquito, the film demonstrates how the salivary glands of the insect are pressed out and prepared for examination so that the sporozoites can be identified. The removal of the stomach and the detection of oocysts are then demonstrated. (Running time, ten minutes.) The second film shows how mosquitoes should be pinned, how to stage and label the pinned insects for permanent display, and how to pack them for dispatch through the post. It was produced in collaboration with the Department of Entomology at the London School of Hygiene and Tropical Medicine. (Running time, five and a half minutes.)

Medical Memorandum

Familial Incidence of Sialectasis

Cases of recurrent swelling of a salivary gland associated with characteristic *x*-ray appearances, and due to causes other than calculus, are seen from time to time. Such cases are described in detail in the literature, but there is sparse reference to any familial tendency, so that the occurrence of the condition in three generations of a family, all treated at Southend General Hospital, is of some interest.

REPORT OF CASES

Case 1.—In 1938 Mrs. X, then aged 50, was seen with a left-sided facial swelling which had been present on and off for 24 years. Until recently she had been able to make the swelling disappear by digital pressure, and stated that the disappearance coincided with the escape of fluid into her mouth. However, in the month prior to admission she had not been able to do this. Examination revealed a swelling in the region of the left parotid gland. It was lobulated and variable in consistency, the upper portion being firm, the lower portion fluctuant. (From a drawing in the case notes, the swelling appears to have been about the size of the patient's ear.) Radiotherapy brought about complete resolution of the swelling, and there has been no further recurrence in the succeeding 15 years. A recent sialogram, however, showed a dilatation of the main duct and some of the smaller ducts, as well as terminal cystic dilatations (see illustration).

Sialogram of Case 1, showing a severe degree of sialectasis with gross dilatation of ducts.

Case 2.—In 1942 Miss X, then aged 26, a daughter of Mrs. X, was seen with a swelling of the right side of the face, present on this occasion for three weeks. She gave a history of having had swellings of both sides of the face at different times since childhood, and had had treatment elsewhere. The parotid gland on the right side was found to be irregular, and was considered to be cystic. There was a discharge of flocculated material from Stensen's duct on that side, and a swab of this material subsequently grew a non-haemolytic streptococcus. A probe was passed up the duct, and no stone felt. The left parotid was slightly lumpy. A course of deep *x*-ray therapy was given with very good effect, and there was no recurrence for six years. An ear infection at that time, associated with some lymphadenitis, caused a temporary flare-up. The patient reappeared in April, 1952, with a recurrence of symptoms—intermittent swelling of one or other parotid gland, which at times was painful. A sialogram done at this time showed dilatation of all the ducts, but to a less degree than her mother's.

Case 3.—A son aged 7 of Miss X, who had married and had three children, was seen in October, 1951, with a history of swellings on both sides of the face, starting several months previously. That on the left side had subsided completely, but on the right side only partially, and tended to recur from time to time. The swelling would sometimes occur during a meal, accompanied by pain, and would subside after an hour or two. A sialogram showed the "snowstorm" appearance characteristic of an early stage of sialectasis, where the finest terminal ductules only are involved.

DISCUSSION

The underlying pathology in this condition, known variously as sialectasis, sialangiectasis, or chronic recurrent parotitis, is obscure, but the essential feature is obstruction of the parotid ducts. Diagnosis is dependent in the final instance on sialography, and the reader is referred to the writings of Payne (1931, 1933) and to the well-illustrated article by Rose (1950) for the technique and description of the sialographic types.

Pearson (1935), discussing the possible mechanism of the swelling, considers that obstruction of the ducts plays a prominent part, either by spasm, oedema, mucus plugs, or epithelial debris, or by the presence of an abnormally viscid saliva. He quotes Steinitz (1929) as a believer in the abnormally viscid saliva theory, and indeed most authors are agreed that the character of the saliva differs from the normal in these cases. Normal parotid secretion is watery, with very little mucus, but the saliva in this condition becomes more mucoid in type and may contain flakes and casts, plugs of mucus and cells, and has been compared with frog's spawn.

Meyer (1934) believed the condition to be due to an acid saliva, and found some improvement with alkali treatment. He also thought that allergy might play a part, and described a case of a boy aged 6 years with parotid swellings associated with the passage of ropy saliva, in whom he obtained positive skin reactions to certain foodstuffs. With the removal of these foodstuffs from the diet the swellings subsided. Sialography in this case showed dilatation of the minor ducts; and it is of interest to note that the boy's mother and his grandmother had a similar condition. No other examples suggesting a familial tendency can be traced in the literature, although two of Pearson's cases were brother and sister. These appeared in a whole series which he described, and, beyond mentioning that they were brother and sister, he made no further comment.

Monro (1951) is another who regards allergy as a main aetiological factor. His case showed a high eosinophil count in the blood and also in the parotid secretion, while the actual blockage of the orifices of Stensen's ducts was brought about by plugs of viscid purulent saliva, observed to be rich in eosinophil leucocytes.

It would seem reasonable to correlate the possible allergic nature of the condition, with its occurrence in different generations of a family as reported here and as described by Meyer, on the grounds of an inherited allergic diathesis, though the occurrence of primary congenital structural changes in cases of sialectasis has not been disproved.

I am grateful to Mr. Rodney Maingot, Mr. Donald Barlow, and Mr. Andrew Monro for permission to publish the above cases, and to Mr. Robert Monro for much constructive criticism in preparing this report.

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The Southend-on-Sea Hospital Management Committee has recently accepted a Trust from Mr. Sydney F. Body, for many years associated with hospitals in the town, expressed in favour of the medical staff of the group of hospitals. The Trust, *inter alia*, provides: (*a*) For an annual lecture to be known as the Sydney Body Lecture to be given by an eminent speaker; (*b*) the award of a medal, not necessarily annually, for merit or research in any approved medical subject in its widest sense. The first Sydney Body medal is to be awarded to Dr. William Evans for his meritorious work in cardiology. Dr. Evans was, until 1946, a consulting physician at the General Hospital, Southend.

Reviews

TEXTBOOK OF OBSTETRICS

A Textbook of Obstetrics. By Professor Bruce T. Mayes, M.V.O., M.B., B.S., F.R.C.S.Ed., F.R.A.C.S., F.R.C.O.G. (Pp. 1,040; 19 coloured plates, 537 illustrations. Price 100s.) Sydney: Australasian Publishing Co. London: George G. Harrap. 1953.

This is a beautiful book which, once the reader has got used to its price, gives pleasure merely to flick over the pages, to glance here and there at the excellent and numerous drawings and photographs, to pause and read a careful description of a nursing brassière or of some day-to-day procedure such as rectal examination, or to become absorbed in the author's asides of personal experience and observation. Even the areas on the abdomen over which the foetal heart is to be heard with greatest intensity are indicated by dots which are heart shaped. How many authors or teachers point out which particular parts of the hands and arms are likely to escape attention during routine scrubbing up, and which become contaminated during drying with a towel? Similar examples of care and devotion to detail, and of art for art's sake, shown by this outstanding teacher could be quoted from almost every page.

The book not only reflects the ability and character of the author, but also the Australian practice of obstetrics, which Professor Mayes does much to encourage by making special reference to any original work carried out in that country. It provides rather more than students in Britain would be expected to know, but its size is accounted for by its wealth of illustrations and spacious type-setting, rather than by digressions into the realms of the specialist.

The author errs on the side of conservatism and hesitates to abandon completely some of the older methods of treatment, such as vaginal packing for placenta praevia and the tape-and-catheter method for replacing prolapsed cord. It is surprising too not to find any reference to the use of penicillin in the treatment of syphilis, to the giving of ergometrine before the delivery of the placenta, even for third-stage bleeding, or to gas-and-air analgesia. But what do these or similar points matter? There is usually more than one way of doing a thing well, and any omission and faults are more than counterbalanced by a host of highly commendable features. Those who learn and practise under the rather different conditions which obtain in Britain, and who have many cheaper textbooks from which to choose, may regard this one as having a spiritual rather than utilitarian appeal. None, however, could deny that it has appeal. It is fascinating: there is even an account of a case of retained placenta successfully treated by injecting the cord with coconut milk obtained from a near-by palm.

T. N. A. JEFFCOATE.

PULMONARY TUBERCULOSIS

Pulmonary Tuberculosis: Pathology, Diagnosis, Management, and Prevention. By Walter Pagel, M.D., F. A. H. Simmonds, M.D., D.P.H., and Norman Macdonald, M.B., M.R.C.P.Ed. Third edition. (Pp. 728; illustrated. £4 4s.) London: Geoffrey Cumberlege (Oxford University Press). 1953.

The third edition of this well-known monograph on pulmonary tuberculosis will be welcomed by everyone interested in the subject. The book is divided into five parts—pathology, diagnosis, prognosis, management, and lastly epidemiology and prevention. The clinician may find the introductory section on pathology tedious and top-heavy, occupying, as it does, more than a quarter of the text. In it the consideration of bronchogenic tuberculosis has been extensively revised, and special attention is directed to the significance of the primary cavity in the young adult.

Physical signs in pulmonary tuberculosis receive scant notice. Indeed, the art of physical examination of the chest, which takes so long to acquire, is now rapidly dying out as more and more attention is given to the *x*-ray findings. I was glad to read in the treatment of haemoptysis that the authors "are not impressed with the argument which favours the withholding of morphine during the bleeding phase, on account of the supposed danger arising out of depression of the cough reflex." Having witnessed the disastrous result which may follow the more modern method of sitting the patient up so that he may cough up the blood, I am inclined to agree. The surgical text has been largely rewritten, although there is now no surgeon included in the team of authors. In some ways I feel this is regrettable, for the surgeon should be able to give a better account of his operations, his reasons for selection of cases, and the factors which may lead to failure, than can the physician.

I have frequently tested the previous edition by using it as a book of reference in clinical work, and have seldom failed to find the information required. The book contains over 300 figures and illustrations, which are extremely well reproduced. I have no hesitation in recommending this edition to the profession. It is an admirable work, a credit both to the authors and to the publishers.

G. E. BEAUMONT.

GENERAL PHYSIOLOGY

General Physiology. By Bradley T. Scheer. (Pp. 613; 110 figures. £2 16s.) New York: John Wiley and Sons, Inc. London: Chapman and Hall. 1953.

Professor Scheer has endeavoured to write a book for the "prospective specialist in biology, including medicine." He has borne in mind the limited time available in the curriculum and has attempted the broadest treatment possible in the circumstances. In so doing he has excluded old or outmoded theories with little relation to present-day concepts. The assumption is made that the work of the student is based on practical experimental work and that he is going to collaborate with Professor Scheer in his experimental rather than a merely textbook approach to physiology.

The book is in five parts—physico-chemical foundations, chemical dynamics, energy transformations, development of organisms, and the integration of the organism. The author sets out well and clearly the basic physical chemistry and the electron theory of atomic structure. Throughout the book he interprets phenomena in terms of atomic structure and valency changes. Avoiding the human, or rather treating the human being as a biological type, the author ranges widely over all the manifestations of life. The book is clear, well written, and can be recommended to anyone anxious to interpret and understand biological phenomena in terms of modern scientific concepts.

A. ST.G. HUGGETT.

SYMPOSIUM ON EVOLUTION

Symposia of the Society for Experimental Biology. Number VII: Evolution. (Pp. 448. £2 5s.) London: Cambridge University Press. 1953.

In this symposium there are twenty-three contributions to the general subject of evolution from many different points of view. The organisms discussed range from bacteria to man and from ferns to butterflies, and the light which their studies throw on evolution serves to emphasize the fundamental unity of the organic world.

There is a masterly introduction by J. B. S. Haldane. He first of all defends mathematical genetics against the criticism of Waddington that "very few qualitatively new ideas have emerged from it." He points out that many ideas "have emerged so completely that their origin is forgotten." Others, such as the findings by Penrose and Haldane that some genes which are deleterious to human beings are kept in being only by mutation, have not yet penetrated far, since the view is still widely held that the human race could be permanently freed from such genes by negative eugenics.

Pringle opens with a discussion of the origin of life; Haldane stresses the fact that recent work on bacteria and viruses indicates that a simple organism "can incorporate and reproduce indefinitely constituents of another by processes which cannot be called sexual." It is possible that two or more kinds of life began independently and then in some way came together. Medawar discusses the remarkable diversity of the antigens found in different members of one mammalian species and the ways in which the dangerous effects on pregnancy have been partly overcome. He makes the important generalization that "endocrine evolution is not an evolution of the hormones but an evolution of the uses to which they are put."

Hinshelwood makes a valuable survey of his recent work on bacterial adaptation, and Demerec contributes a paper on the reaction of genes of *Escherichia coli* to certain mutagenic agents, such as manganous chloride and ultra-violet rays. Other notable papers are on the genetical structure of populations (Mather), stochastic processes and the growth of bacterial colonies (Kendall), and epigenetics and evolution (Waddington).

The juxtaposition of factual information from so many points of view in a rapidly growing field renders the volume invaluable to the general biologist interested in evolutionary mechanisms. The British Council and the Rockefeller Foundation are to be thanked for financial aid towards the cost of publication.

S. C. HARLAND.

BIOASSAY OF HORMONES

Ciba Foundation Colloquia on Endocrinology. Volume V: Bioassay of Anterior Pituitary and Adrenocortical Hormones. Edited by G. E. W. Wolstenholme, O.B.E., M.A., M.B., Ch.B., assisted by Margaret P. Cameron, M.A., A.B.L.S. (Pp. 228; 53 illustrations. 25s.) London: J. and A. Churchill. 1953.

This is one of twelve informal colloquia that have been arranged by the Ciba Foundation and subsequently published under the editorship of Dr. G. E. W. Wolstenholme, with the assistance of Miss Margaret Cameron; recordings of the discussions were made by Miss N. Bland. The usual high standard to be expected from Ciba Foundation publications is here conspicuous throughout, and this has been found to be by no means incompatible with the "house party" atmosphere which the preface says has been attempted at all such conferences. The contributors come from widely separated groups, but they are studying common problems of assay of the pituitary and adrenal hormones. The results are of interest to all research workers and to research-minded clinicians.

There is an initial discussion on the requirements for clinically useful endocrine bioassays by Albert Segaloff, of New Orleans. The section on thyrotrophic hormone considers bioassay in the hypophysectomized rat using P^{32}; assay by iodine^{131} (by Gilliland and Russell Fraser of the British Postgraduate Medical School); and chick assays using P^{32} by A. C. Crooke and Joyce Matthews, of Birmingham University. The section on gonadotrophins is illuminated by an excellent record of original work by W. R. Butt and A. C. Crooke on chromatography of urinary gonadotrophins. The clinician will be interested to find a chapter on their clinical use and clinical applications. E. B. Astwood, of Boston, discusses biological tests for luteotrophin as a basis for assay. Discussions on prolactin, including conventional methods of assay, and the assay of urinary prolactin are included in this section.

In section four, on the bioassay of growth hormone, C. H. Li considers the well-established procedures such as weight in normal plateaued rats, hypophysectomized rats, and dwarf mice, increase in tail length of hypophysectomized rats, and increase in width of epiphysial cartilage of the tibia of such rats. Also discussed is the use of radioactive tracers to investigate increase in liver weight, change in nitrogen constituents of the blood, change in serum phosphorus and phosphatase, change in nitrogen and phosphorus balance, and increase in protein synthesis. E. Reid, of Cambridge, considers the assay of growth hormone for diabetogenic activity, a field in which the Cambridge Biochemical School have been pioneers.

Perhaps the most interesting sections are five and six, on adrenocorticotrophic hormone and adrenocortical hormones. In particular I should like to mention the important contribution by C. H. Gray and D. M. V. Parrott on the measurement of A.C.T.H. activity in plasma by the depletion of ascorbic acid in the adrenal cortex of the hypophysectomized rat. Ingle reviews the recent work done in his laboratory on the effect of adrenalectomy and adrenal steroids on muscle work. Marthe Vogt discusses observations on comparative biological assays of adrenal cortical steroids. J. A. Nissim, of Guy's, considers the assay of glucocorticoids, with liver glycogen estimations in mice and rats. Bush writes a most important section on paper chromatography of steroids, in which he has played such a leading part, and the application of this method to assay problems. J. H. Gaddum, of Edinburgh, brings his wisdom to some invaluable closing remarks.

S. L. SIMPSON.

DERMATOLOGY IN GENERAL PRACTICE

Dermatology in General Practice. By Jacob Hyams Swartz, M.D. Foreword by Professor C. Guy Lane, M.D. (Pp. 581; 253 figures. £4 4s) London: Baillière, Tindall and Cox. 1953.

It is not possible in the compass of five or six hundred pages to give anything like a complete account of all the diseases of the skin, and the problem of pruning is one to which an author of a textbook for non-dermatologists must find his own solution. Dr. Swartz, in this book, has aimed at making some mention, however brief, of all the dermatoses; he has left very few disorders unnamed, though his descriptions of some of the rare ones are perforce often little more than can be found in a medical dictionary.

After a very short introductory section on the anatomy and physiology of the skin and a longer section on the care of the skin, the main part of the book consists in the description of individual disease pictures classified according to regions. This part of the book follows the orthodox lines which have been familiar in textbooks for several decades, and there is little that is new on diagnosis and aetiology. It is perhaps desirable to be dogmatic in a work of this kind, but many of Dr. Swartz's statements are so highly controversial that the dermatologist can hardly leave them unchallenged. For example, acne varioliformis "is probably a tuberculide" requiring, one may observe, the treatment of "hygiene, large dosages of vitamin A, and a high protein diet" (p. 97).

The author's account of treatment is, on the whole, well done and it records plentifully his personal preferences, but there is no mention of isonicotinic acid hydrazide for tuberculosis, nor of mepacrine for lupus erythematosus. This is not because the book is out of date, for cortisone, A.C.T.H., and the antibiotics are given very adequate consideration. The book includes a long section on mycotic infections, of which the author has made a special study, and a chapter on syphilis. Treatment by irradiation is briefly mentioned, the antibiotics are reviewed, and A.C.T.H. briefly considered. Finally, there is a practical formulary of over 30 local applications written in a confusing combination of English and doubtful Latin. It is noticeable that the author has but little use for the modern emulsifying bases.

Notwithstanding these criticisms, this should be a useful book. It includes a good deal of information not usually presented to the general practitioner, it is clearly written and profusely illustrated with photographs which are on the whole good. It is doubtful, however, whether there is anything about this book which presents a serious challenge to others of its kind already well known in Britain.

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MOUSE CARCINOGEN IN TOBACCO TAR

The experimental production of skin carcinoma in mice by painting them with cigarette tar has been performed in the U.S.A. by Drs. E. L. Wynder, E. A. Graham, and A. B. Croninger. The results are to be published soon.[1] Some indication of the size of the lung cancer problem in England and Wales now may be seen briefly by comparing some death rates. In 1900 the crude annual death rate attributed to lung cancer was 8 per million persons. Fifty years later it had increased to 278 per million. In 1950 the disease caused 12,241 deaths, a total which comprised 24% of all cancer deaths in men at all ages and 40% in men of ages 45–54. The increase, which has continued since and seems likely to do so in the future, is only in very small part due to the increasing proportion of the population who live to the ages of higher cancer susceptibility. If part is due to better diagnosis, not the whole increase is spurious, and in Doll's moderate opinion[2] the real increase may well be more than half. As Doll points out further, the importance of this conclusion is that it holds out hope for prevention, for an increase of such extent and rapidity is almost certainly due to a potent environmental factor. The earlier conclusions of Doll and Hill in Britain,[3] and of Wynder and Graham in the United States,[4] did not at first obtain universal endorsement, partly because of a proper scientific caution, and partly for human reasons of a different kind, but the intervening three years have seen a growing acceptance, first, that the reported increase in incidence is real, and secondly that its major cause is smoking. Doll was the first to acknowledge that no proof is ever absolute, and that only by further experiment can confidence be increased until finally the truth is unquestioned.

The study by Wynder and his colleagues of the production of carcinoma with cigarette tar is an important contribution. They conclude from a survey of the literature that all previous attempts to induce cancer in mice with tobacco products were successful in the production of only seven epidermoid cancers of the skin—a poor result, perhaps due in part to inadequate methods and too short a period of observation. In their own investigation a tar condensate, obtained by smoking a popular brand of cigarette in an apparatus designed to simulate human smoking methods, was applied in relatively large quantities, and over a long period, to the skin of mice (of the CAF_1 line). Of 81 mice so treated, 36 developed epidermoid cancer of the skin after a mean time of 71 weeks. This is a long latent period amounting to about half the life span of the animals used, and the rather moderate activity of the tar is shown by a parallel experiment in which 25 mice treated in the same manner with a solution of methylcholanthrene all developed carcinomata within 18 weeks. No tumours were observed in a control series treated with the solvent (acetone) alone.

What is the significance to be attached to these experiments? The fact that carcinogenicity had not hitherto been very clearly demonstrated as a property of cigarette tar did not invalidate the evidence already existing to incriminate tobacco. Equally, on the other hand, it cannot be claimed that the new results —suggestive as they are—afford any formal proof that the agent in cigarette tar which is capable of inducing cancer in the skin of mice is necessarily responsible for the increased incidence of bronchogenic cancer in man. Their true significance would seem to be rather that they represent an effort, made in accordance with the general acceptance of the nature of the risk and its almost certain cause, to identify the latter with precision. If the actual carcinogenic or possibly co-carcinogenic agents in tobacco remain to be identified it may be noted that no spectroscopical evidence of the presence of 3:4-benzpyrene was found by Wynder's associates, in agreement with a similar observation by Waller.[5] Subject to the provisions made above, the new results might also be thought to increase the unlikelihood that arsenic is the carcinogenic agent, since this is incapable of inducing cancer on application to the skin of animals.

The present developments must not be allowed to obscure the wisdom of Doll's view, that it may be unnecessary to await the isolation and identification of a specific carcinogenic agent before doing something to halt the rapid increase in mortality and to turn it into an even more dramatic decline. Few now doubt that abolition of the cigarette, or abstinence from its use, would be the most beneficent single step in cancer prevention available to us to-day. Short of this ideal, research will assuredly continue, and indeed should be promoted with much increased vigour, to identify the cause and allow prevention by its removal. Finally, the question arises whether the

[1] In *Cancer Res.*, 1953.
[2] Doll, R., *British Medical Journal*, 1953, **2**, 521, 585.
[3] —— and Hill, A. B., ibid., 1950, **2**, 739.
[4] Wynder, E. L., and Graham, E. A., *J. Amer. med. Ass.*, 1950, **143**, 329.
[5] Waller, R. E., *Brit. J. Cancer*, 1952, **6**, 8.

combined weight of evidence is now so compelling as to convince the tobacco industry itself that there may be some connexion between tobacco and cancer of the lung.

RADIOLOGY AND LUMBAR DISKS

It is now about twenty years since it became recognized[1] that sciatica is nearly always caused by a protrusion of either the fourth or fifth lumbar intervertebral disk pressing on the fifth lumbar or first sacral nerve root. Though this observation may seem simple to-day, an enormous "disk" literature has grown up. This alone suggests that all the problems are not yet solved, and indeed opinions still differ widely on diagnosis, treatment, and prognosis.

While it is generally conceded that radiology is important in diagnosis, many authorities disagree sharply on how important, and particularly do they disagree about contrast radiography. The necessity for taking plain radiographs of the lumbo-sacral spine is universally agreed. But it must be emphasized that this investigation is chiefly of use in narrowing down the differential diagnosis, and in particular excluding a more serious lesion such as a metastasis or tuberculous infection. Even so, such gross pathological lesions as these, though usually easily recognized at operation or necropsy, may not appear on the best radiographs—including tomographs.[2] Radiology is a rather insensitive test, and often bony destruction is considerable before it is visible. Serial radiography is therefore necessary in a case of sciatica that does not respond to conservative therapy.

While plain radiographs convey limited yet indispensable information, too much must not be read into them. Some doctors who see scores of disk lesions every year become very astute in their clinical diagnosis and probably achieve an accuracy of over 90%. Having made a confident and usually correct clinical diagnosis, they are tempted to demonstrate the site of the offending disk on the radiograph. The only occasion on which a protruded disk can be seen on a radiograph is when it is calcified. Unfortunately this type of degeneration is almost unknown in low lumbar disks, though curiously common in the relatively very rare protruded thoracic disks.[3]

There are certainly some radiological signs suggestive of disk protrusion, but they may be dangerous if they lull the physician or surgeon into even greater confidence in his already firm clinical diagnosis. Here two points are relevant. The first is that the volume of a lumbar disk is 10 ml. or more. If less than one-tenth of it protrudes, it is sufficient to press hard on a nerve root and cause intense sciatica. Such a small diminution in total disk volume will be quite undetectable on a radiograph. The second point is that disks desiccate. This is common in old age. When desiccation occurs, backward protrusion by no means necessarily follows, but radiographically the disk space becomes much narrowed and secondary osteoarthritic changes usually appear. Thus a normal disk space does not exclude the diagnosis of a protruded disk, and a grossly narrowed space is not proof of protrusion.

Four out of five cases get better when treated conservatively, and an even higher proportion of cases of lumbago are restored to health,[4] but for the residue of cases surgery is usually the treatment of choice. The fact that it is not always—even though very often—as dramatically successful as drawing a tooth has been largely responsible for the mass of literature on the disorder. And, just as occasionally the cause of the pain is not a tooth at all, so with disks. Myelography helps in diagnosis, but it has the more important function of revealing a tumour—usually benign—which may lie several inches higher up the spinal canal and be quite invisible at low lumbar laminectomy.

In many centres in Britain there is a prejudice against myelography, especially among orthopaedic surgeons. Their distaste for all contrast media, gas or liquid, is great. The opinion is sometimes expressed that the method is not without danger and that serious sequelae, especially arachnoiditis, are common. Again, no contrast substance, even with the best technique and interpretation, reveals all protruded disks. And critics also contend that the procedure is not only harmful but redundant, since clinical diagnosis is so accurate. On the other hand, at most neurological centres in this country myelography is held to be an essential investigation. At the Lahey Clinic 4.3% of 1,104 cases operated upon for supposed disk lesions were tumours of the cauda equina.[5] Love[6] reported that eight spinal tumours, whose signs simulated those of disk lesions, were removed at the Mayo Clinic during the same period as 100 disk lesions were operated upon. And Barr, co-author of the paper drawing the attention of the world to the true cause of most cases of sciatica, whose opinion cannot lightly be dismissed, has said that there is only one way by which catastrophes can be avoided—routine myelography.[7]

1 Mixter, W. J., and Barr, J. S., *New Engl. J. Med.*, 1934, **211**, 210.
2 Knutsson, F., *Brit. J. Radiol.*, 1953, **26**, 113.
3 Logue, V., *J. Neurol. Psychiat.*, 1952, **15**, 227.
4 —— *Postgrad. med. J.*, 1953, **29**, 234.
5 Toumey, J. W., *et al.*, *J. Bone Jt Surg.*, 1950, **32A**, 249.
6 Love, J. G., *J. Neurosurg.*, 1944, **1**, 275.
7 Barr, J. S., *J. Bone Jt Surg.*, 1950, **32A**, 266.

SELF-HELP AND PUBLIC HEALTH

We get used to hearing year by year that the health of the nation improves, so it is timely of Sir John Charles to remind us in his latest report[1] that "it is not sufficient that the man in the street should rest in a quiet acceptance of all the benefits of a steadily improving environment as if they were part of nature's boundless provision." Nature's provision is far from boundless, as is apparent to the man in the fields if not to the man in the street, and even the State's provision is the more effectual for co-operation from the people using it. But in spite of disastrous flood and fog in 1952 the citizens of England and Wales remained remarkably healthy—if the inference may be drawn from figures for notified diseases and registered deaths. Outstanding among the diminishing causes of death is tuberculosis: the death rate from all forms was 240 per million, a conspicuous fall from the average figure of 535 per million for 1945–9. By contrast 1952 was notable for deaths from cancer of the lung (14,218) much exceeding those from all forms of tuberculosis (10,585). This reversal owed more to the fall in tuberculosis deaths than to the rise in lung-cancer deaths, but the latter seem to be increasing uninterruptedly even so. We discuss elsewhere (p. 1362) some new American work on the production of experimental cancers in mice by tobacco-smoke extract, and it seems that those who are yet unconvinced of any connexion between smoking and cancer of the lung are being left increasingly little space to manœuvre in. Another severe disease on the increase is leukaemia, with 2,043 deaths. The death rate from it has been rising for many years, and it is hardly likely that improving diagnosis can be responsible, at least for all the increase. Mortality was 74% higher than in 1938, and the comparative mortality index in the five years 1948–52 (with 1938 mortality taken as 1.00) rose as follows: 1.32, 1.50, 1.58, 1.66, and 1.74.

The figures for admissions to mental hospitals continued to increase, there being 62,258 in 1952 as compared with 59,288 in 1951 and 27,979 in 1939. But this does not necessarily imply that there are more mentally disordered people; the likelier explanation is that people nowadays more readily seek or agree to admission than formerly. Again, the number of mental defectives under guardianship and on the books of hospitals continued to rise, being 62,704 in 1952, about 1,000 more than in the previous year. But the increase is probably due to the growing recognition of mental defect as a clinical condition and social problem, and also to increasing difficulty in assimilating these people into society as industrialization spreads.

Referring to tasks that parents should be undertaking on behalf of their children, Sir John Charles finds that they are failing in their duties in some respects. "Infant vaccinations against smallpox are 70% less than they should be, and for both diphtheria and smallpox the proportion who have their immunity maintained by reinoculation or revaccination is deplorably low." Further, "the same sorry tale of parental carelessness is to be recounted in relation to dental care," and "there is something very far wrong when more children under 15 years of age die from accidents in their homes than are killed on our congested thoroughfares." The uptake of Government-provided orange juice and cod-liver oil for infants is "less than half of what it should be." There are these and other signs in this admirable report that a great many people would be better employed making some slight efforts on behalf of themselves and their children instead of crowding consulting-rooms and hospitals to repair the health they have allowed to decay from neglect.

[1] *Report of the Ministry of Health for the Year Ended December 31, 1952*. Part II. 1953. H.M.S.O. 6s. 6d.

THE MANAGEMENT OF ULCERATIVE COLITIS

None of the theories put forward to explain the aetiology of ulcerative colitis has yet led to a logical and generally effective regime of treatment. The management must therefore be based on a sound application of general principles; and in assessing the effect of the various measures adopted there is no disease in which it is more important to bear in mind the background and natural course of the malady. Wittkower[1] found that in most of these patients psychological abnormalities were present before the colitis began, and it is now widely recognized that they are people characterized by emotional immaturity, often having a pathological parental attachment and perhaps being extremely meticulous and fussy. Successful results from psychotherapy have been claimed by Daniels.[2] And, although the more generally held view is that only transient benefit, if any, can be expected from such treatment, it is nevertheless true that the medical care cannot be planned to best advantage without an understanding of the psychological situation and of the various emotional crises which often initiate relapses. No one is as well placed as the family doctor to evaluate these environmental factors; and it is on a correct appraisal of them, and by taking into account the possibilities of satisfactory adjustment of emotional problems, that the best estimate of the prognosis of an early case may perhaps be based.

In planning the details of treatment it is well to remember certain general considerations. At the best the illness is likely to last for many months, and acceptance of this fact by patient and doctor is the first step towards successful management. On the other hand, although remission followed by relapse is the usual sequence, apparently complete and lasting recovery is not unknown, and for this reason alone the patient should not be subjected too early to mutilating surgery. This is not to say that operation should be reserved for the moribund; selection at the right time of the right patient for ileostomy and perhaps colectomy requires the co-operation of physician and surgeon and taxes the judgment of both. Elsewhere in this issue Mr. S. O. Aylett recommends, for suitable cases, an operation which preserves rectal function. It is now fashionable to advise rather earlier surgery, which in our present ignorance is probably correct; but many will echo the words of Marino,[3] who said that the more ileostomies he per-

[1] *British Medical Journal*, 1938, **2**, 1356.
[2] *Med. clin. N. Amer.*, 1944, **28**, 593.
[3] *J. Amer. med. Ass.*, 1947, **133**, 1001.
[4] Hoffbauer, F. W., *et al. Ann. intern. Med.*, 1953, **39**, 267.
[5] Bargen, J. A., *ibid.*, 1953, **39**, 285.

formed the more he wished there were some other method of caring for these patients. In the medical treatment there is general agreement only about the necessity for complete rest, which should be continued as long as there is fever or more than two or three stools in 24 hours. Almost equally important, in view of the drain of protein from the bowel and the common occurrence in the liver of fatty change or even cirrhosis,[4 5] is a high-protein diet. An adequate intake can nearly always be assured by the addition of concentrated supplements such as soluble casein. At least in the active phases fruit and vegetables must be largely excluded from the diet, and for this reason vitamin C and the B complex must be given in full doses. Anaemia is always present, and, though it may respond to the administration of iron by mouth, transfusion often seems to be of general benefit in addition to raising the haemoglobin level and should not be reserved only for the severely anaemic. During acute exacerbations courses of phthalylsulphathiazole and aureomycin by mouth, and penicillin by injection, should be tried, though they rarely cause dramatic improvement. Again A.C.T.H. or cortisone have occasionally appeared to initiate remission in a fulminating case, but usually have little or no effect. For relief of painful colon spasm associated with wind there is probably nothing better than a tablespoonful of charcoal and 5 minims (0.3 ml.) of tincture of belladonna three times a day, the dose of the latter being gradually increased to the limit of tolerance. The present tendency is to regard colon wash-outs as of very limited value. In conclusion it may be reaffirmed that most success in the management of this distressing disease attends those who are best able to bring continued hope, encouragement, and support to the rather inadequate and dependent sufferer.

NIGHT WORK AND SHIFT CHANGES

The effects that night work and shift changes have on output and absence from work were the subject of a recent investigation carried out by the Medical Research Council Group for Research in Industrial Psychology.[1] For the most part the results confirm the work already done in this field, but they may come as something of a surprise to readers not already acquainted with it. The most striking fact is that there is very little difference in the rates of output on day and night shifts. In two of the ten factories with which the inquiry was concerned, the output from the night shifts was in fact very slightly the higher. This may be explained away, but the fact remains that the comparative ratio in output between day and night shifts was shown to be only of the order of 101 : 99.

The evidence shows, however, that there are features of night work which need to be more carefully borne in mind than they are at present. The article contains an impressive table showing that the percentage of absence uniformly falls week by week while day work is continued, and uniformly rises week by week when a shift changes over to night work. Moreover, the opinions expressed by the members of a sample of workers who were interviewed showed, as might have been expected, that night work was highly unpopular. Digestive troubles and sleeplessness were much complained of, and it is noteworthy that, out of the 150 men in the sample, no fewer than 65 took patent medicines every day or several times a week. The types taken suggest, it is said, that they were relied on "to counteract disorders of the stomach."

The authors sum up by saying that "there is not the least doubt that night work is unpopular and in the long run is detrimental to health, efficiency, and the enjoyment of life. In every group of workers, some break down in health after a few weeks, months, or years of night work. . . . Almost all workers are adversely affected in some degree." This may be thought to be a somewhat strong conclusion in view of the evidence on which it is based in this paper. Adverse comparisons between day and night work in regard to output and lost time have been difficult to make since the Health of Munition Workers Committee presented its report in 1918. Moreover, so far as shift working in general goes, the Ministry of Labour has just reminded us that Departmental Committees reported in 1934 and 1945 that they were unable "to discover any grounds for supposing that [it] increases sickness rates or the incidence of digestive or nervous disorders," though the familiar effects on family and social life were again reported on, especially in 1945. But it seems to be obvious that the serious disturbance in the pattern of daily life which shift work brings with it must have its physical effects, provided it is done over a long enough period. It is therefore to be hoped that this research will be continued by following up a sample of cases over a decade or so.

CHELATION

Chelating agents, like exchange resins, are yet another of the tools which the industrial chemist has passed on to the physician. The word chelation (χηλή, a claw) indicates the ability of certain chemicals to donate atoms —usually oxygen, nitrogen, or sulphur—which will form co-ordinate bonds with polyvalent metallic ions: the result is a stable, water-soluble, non-ionic metallic "ring" in which the metal is firmly held.[1] It is important to note that the resulting compound is not precipitated. The avidity of a chelating agent for a particular metal varies. For example, lead is more strongly bound than calcium and will displace the latter from a chelated complex. The best known of these agents in practical use is ethylenediamine tetracetic acid (E.D.T.A.) (marketed commercially as "versene," "sequestrene," "trilon," "nullapon," etc.), though citric, malic, lactic, and tartaric acids are all natural chelating agents, and both chlorophyll and haemoglobin are examples of chelated complexes.

The possible uses of chelation are very numerous. It is already used in industrial processes as varied as the softening of water (by removing calcium), the removal of trace metals from dyes to improve colour, the

1 Wyatt, S., and Marriott, R., *Brit. J. Industr. Med.*, 1953, **10**, 164.

1 Walton, H. F., *Sci. Amer.*, 1953, **188**, 68.
2 *Arch. Industr. Hyg.*, 1953, **7**, 137.
3 Ibid., 1953, **7**, 148.
4 *Science*, 1953, **117**, 659.
5 Aheshouse, B. S., and Weinberg, T., *J. Urol (Baltimore)*, 1951, **65**, 316.
6 Gehres, R. F., and Raymond, S., ibid., 1951, **65**, 474.
7 Proescher, F., *Proc. Soc. exp. Bio. (N.Y.)*, 1951, **76**, 619.

preservation of food, the improvement of soils (humus contains chelating agents which bind iron and calcium), and the removal of traces of radioactive substances. As for the uses of chelation in medicine, lead poisoning is an obvious indication; and a recent conference[2] was called at the Massachusetts General Hospital to discuss the possibility of using E.D.T.A. in this condition. Animal studies have confirmed its ability to remove such ions as calcium, lead, yttrium, and plutonium, and if given in the acid form it rapidly causes fatal hypocalcaemic tetany. In therapy, therefore, the calcium salt should be used; this appears to be non-toxic and is not broken down, 95% being recoverable from the urine. The suggested daily dose is 1 g. per 30 lb. (14 kg.) body weight in a 3% solution intravenously for five days, followed by a rest period. Preliminary reports by Foreman[3] and Rubin[4] and their collaborators suggest that calcium E.D.T.A. may be effective during acute exacerbations of lead poisoning in man. Moreover, this form of treatment has an added advantage in that no free ions are liberated in the mobilization of lead. How much of the metal can be removed from the bones has yet to be determined, but animal experiments are encouraging.[2]

Chelation may have a use in arsenic and mercury poisoning. Foreman and his colleagues gave calcium E.D.T.A. to a patient with berylliosis, though with little obvious effect. E.D.T.A. has also been instilled into the bladder and renal tract to dissolve stones with some success,[5,6] but it tends to cause severe mucosal irritation unless used in a very dilute solution. Proescher[7] has shown that very small amounts of E.D.T.A. will preserve blood for long periods without danger, and it has obvious uses as an anticoagulant. There are many other possible applications, both therapeutic and experimental, for these versatile substances.

LOUSE INFESTATION

The extent of infestation in the towns of England and Wales had scarcely been realized until the wartime evacuation scheme brought many householders in the reception areas into unaccustomed contact with the problem. Mellanby carried out an investigation into the prevalence of the head louse in England on behalf of the Board of Education,[1] and later published results of a four-year survey ending in September, 1943.[2] He found, generally speaking, that there was a considerable variation in the incidence of head lice in different age groups, in the two sexes, and in different areas. As the result of intense activity by various officers of the health services during the next few years, infestation by lice and nits seems to have been reduced. "Nevertheless," wrote Mellanby, "in our industrial cities nearly 50% of preschool age children of both sexes and of school girls are verminous. Older girls and women are the only section of the population which has become lousier during the war."[2] The Chief Medical Officer of the Ministry of Education, discussing[3] this problem, mentioned that Lieutenant-Colonel Madock carried out an investigation in 1947 similar to Mellanby's of 1942–3. It is a grave reflection on the cleanliness of our urban population that 18.2% of patients admitted to a group of hospitals (the same as reviewed by Mellanby earlier) were in 1947 reported by competent nursing staff to be infested. At the end of this account the infestation of problem families is specially described and the use of a family service unit commended. But surely this is carrying the Welfare State too far; while some encouragement is desirable, at least the parents might be expected to keep the family reasonably clean. Ewan[4] has stated that 11.1% of 51,349 children examined at routine medical inspections had unclean heads, and he also quoted similar figures from the statistics of other Scottish education authorities. The rates of infestation in the different wards of the city or in the different categories of schools in Glasgow are not given, but in other areas there is evidence to show from the results of routine examinations for cleanliness, particularly those carried out on the reopening of schools after the Christmas holiday, that in certain schools up to 45% of the girls in attendance may be shown to be lousy or to have nits.

Recent reports have emphasized the family as the unit of infestation. Ewan, for example, has asked that the medical officer of health for the city should be directed to apply for the reintroduction of legislation similar to the Scabies (Scotland) Order, 1941. This wartime regulation had its counterpart in England, and gave the medical officer of health power to inspect premises, to examine persons accommodated in these premises, and to compel verminous persons irrespective of age to submit themselves for cleansing. These orders resulted in the virtual disappearance of scabies; simultaneously the number of persons found to be verminous was reduced considerably.

Infestation is particularly noticeable in the second-generation immigrants in various urban areas, and the real administrative difficulty in controlling it now lies not in the cleansing of schoolchildren, which is easily carried out under the provisions of the Education Act, 1944, but in the fact that the mothers and sisters of the affected children form reservoirs of infestation. Attempts to eliminate it are frustrated by lack of powers to treat relatives in the homes. There is no power under which medical officers of health either in England and Wales or in Scotland can force persons suspected of being lousy to submit to examination, though the Public Health Act of 1936 (Section 85) authorizes him to enter premises and to deal with articles as well as the fabric of the premises if these inanimate objects are affected by vermin. There is a strong case for giving the medical officer of health powers similar to those in the Scabies Order, which ceased to be operative in 1947.

Persuasion has been tried and found wanting; home visits, either by school nurses or by the sanitary staff of the local authorities, have not been adequate to eliminate the hard core of infestation. It is surely time that the freedom of the louse to breed in a small but troublesome number of dwellings in this country was finally curtailed.

1 Mellanby, K. *Med. Offr*, 1941, **65**, 29.
2 —— Ibid. 1943 **65** 205.
3 *Hlth Sch. Child.* 1950 1 H.M.S.O.
4 *Glasgow Herald*, September 24, 1953.

CLINICAL PATHOLOGY IN GENERAL PRACTICE

GLYCOSURIA AND HYPERGLYCAEMIA

BY

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Glycosuria and hyperglycaemia are closely related because, except in those patients with a lowered renal threshold, glycosuria is always an indication that the blood sugar is higher than normal. While recent advances in our knowledge of renal physiology have invalidated the concept of a renal threshold as an unvarying and characteristic concentration of glucose in the blood—above which glycosuria occurs, and below which it does not—there is no doubt that from the clinical point of view this concept is justified and of real value. In most people the renal threshold is about 180 mg. per 100 ml., a value which the blood sugar normally never exceeds; glycosuria does not therefore occur. Hyperglycaemia with a blood-sugar concentration exceeding the normal threshold, as occurs in diabetes and in a few other pathological conditions (see below) leads to the appearance of sugar in the urine. In patients with a normal renal threshold glycosuria is absent when the blood sugar is below 180 mg. per 100 ml., a trace is detectable when the sugar concentration is around 200 mg. per 100 ml., while a complete reduction of the usual clinical testing reagents is given when the blood sugar is 300 mg. or more per 100 ml.

Glycosuria can, however, also occur without a raised blood sugar in renal glycosuria, in which condition the renal threshold is lower than normal, being sometimes as low as 80 mg. per 100 ml. The threshold is sometimes raised, especially in diabetes; hyperglycaemia with blood-sugar concentrations above the normal threshold can then occur without glycosuria.

Tests for Reducing Substances in Urine

The presence of a reducing substance in the urine may be investigated by Benedict's test* or by the recently developed "clinitest" tablet test. Fehling's test is less sensitive and less specific and has little to recommend it. Benedict's test is less easy to perform properly than the clinitest, which has many advantages in general practice because no external source of heat is required. The very rapid and convenient screening test using clinitest with undiluted urine is especially valuable, but a positive result should always be confirmed by the standard technique recommended by the manufacturers.

Significance of Reducing Substances in the Urine

The urgency with which the general practitioner must act upon finding that the urine of his patient reduces Benedict's solution or the clinitest tablet must depend entirely upon the clinical condition. Most patients with diabetes mellitus give a clearly defined history of the disease, and if a positive test for reducing substances in the urine is found in a patient with loss of weight, pruritus, thirst, and polyuria there is no point in arranging elaborate investigations to decide whether or not the reducing substance is glucose. The problem of the moment is whether the patient has diabetes, and, if so, whether the condition is an urgent one requiring immediate treatment with insulin. This will depend on the presence or absence of severe ketosis.

Reducing Substances and Ketone Bodies in the Urine.—As soon as a urine is found to contain a reducing substance, Rothera's test* for acetone and aceto-acetic acid should be performed. If it is strongly positive it should be followed by Gerhardt's ferric chloride test* for aceto-acetic acid. The Rothera reaction is much more sensitive than the ferric chloride reaction, and when the latter is positive the ketosis is more severe. Much care, however, must be taken in the interpretation of the ferric chloride test; patients who have been unwell have often taken salicylates or aspirin previously, and the distinction between the colour reaction given by salicylates in the urine and that given by aceto-acetic acid is by no means as clear-cut as many books suggest. The classical means of distinguishing the ferric chloride reaction due to salicylates from that due to aceto-acetic acid is that the latter reaction becomes negative after boiling the urine, but this is hardly ever necessary, because the patient himself will be able to say whether he has had aspirin or salicylates. A positive ferric chloride reaction due to aceto-acetic acid will be accompanied by an extremely intense Rothera reaction which will be negative if the reaction is due to salicylates.

Some difficulty might be expected if there is severe ketosis and the patient has had either of these drugs, but the presence of heavy glycosuria and ketone bodies in the urine, together with such evidence of pre-coma as recent vomiting, shortness of breath, abdominal pain, giddiness, and acetone in the breath, must be taken as an indication for immediate treatment with glucose and insulin. It may indeed be dangerous to wait for a blood-sugar determination unless facilities for this investigation are readily available. It is the opinion of those with special experience that patients in diabetic coma or pre-coma are best treated in centres with facilities for the control of this condition. All that is required, therefore, is that the patient should be given a dose of 40 units of insulin, together, if possible, with 50 g. of glucose by mouth, and then sent to hospital. In the absence of clinical signs of pre-coma a blood-sugar determination may also be dispensed with in reaching a diagnosis of diabetes if the history is typical and reducing substances and ketone bodies are present in the urine.

Reducing Substances Without Ketone Bodies in the Urine.—Matters may be very different when there are no ketone bodies in the urine. Even then the case with a classical clinical history of diabetes requires little in the way of further investigation, although it is wise never to treat a patient as a diabetic without at least one definitely abnormal blood sugar. For this reason it is unwise to institute treatment in those cases without ketosis before confirming the diagnosis. A blood sugar should be done one and a half to two hours after a full carbohydrate meal, when a figure greater than 180 mg. per 100 ml. is certainly indicative of true diabetes. However, as is shown below, the value of the single blood-sugar determination, although excellent when the blood sugar is definitely raised, is of less value when the concentration is only slightly above the upper limit of normal or when the relationship between the collection of the blood and the time and nature of the previous meal is uncertain.

On the other hand, if on clinical grounds the practitioner thinks that the diagnosis of diabetes mellitus is unlikely, a single determination of the blood sugar *may* help, but it is usually essential to carry out a glucose-tolerance test. It is always worth while looking for glycosuria in two samples—the early morning sample passed before breakfast and the

*See also the article in this series by Dr. H. E. Archer on "Urine Testing in the Surgery" (November 28, p. 1211).

sample taken one and a half hours after a full carbohydrate meal; glycosuria is most likely to be present and heaviest in this second sample. If in a patient not receiving insulin the amount of reducing substance in the urine is not greatly increased about one and a half hours after a carbohydrate meal, the reducing substance is unlikely to be glucose.

The identification of a reducing substance in urine is very seldom required. The value of the osazone test and of the yeast fermentation tests in distinguishing glycosuria has been over-emphasized. The osazone test is difficult to carry out, and even in the hands of the experts is not always as reliable as has hitherto been believed. Fermentation tests, too, are not always satisfactory, for many of the common varieties of yeast ferment sugars other than glucose. The recently developed paper chromatographic method of detecting and identifying reducing substances in the urine is by far the most satisfactory yet devised. With this technique it has recently been shown that in pregnancy lactosuria is twice as common as glycosuria, the former being found in as many as 50% of the antenatal patient attendances. All things considered, the identification of a reducing substance in urine should be undertaken by laboratories specializing in this kind of investigation.

A Single Determination of the Blood Sugar

In many cases of diabetes, even in those in which the clinical history is not entirely typical, the diagnosis may be definitely established by the determination of the blood sugar. The interpretation of the result obtained depends upon the knowledge of the effect of the previous meal upon the blood-sugar concentration. It is shown below that after 50 g. of glucose in the fasting condition the blood sugar normally rises from a fasting level of 80–100 mg. per 100 ml. to not more than 180 mg. per 100 ml. and returns to normal within two to two and a half hours of the beginning of the test. When instead of having 50 g. of pure glucose the food consists of an ordinary mixed meal the blood glucose will not rise quite so high but will take a longer time to return to normal. After a breakfast consisting of eggs and bacon and two or three slices of bread with butter and marmalade, the blood sugar may rise to 140 or 150 mg. per 100 ml. and yet take up to three hours to return to the fasting concentration, whereas after a typical tea of bread, butter, jam, and cake, conditions will approximate more closely to the events occurring in the glucose-tolerance test. It is clear, therefore, that with a typical clinical history a single blood-sugar determination, taken one and a half to two hours after a meal, giving a result above 150 mg. per 100 ml. will almost certainly establish the diagnosis. On the other hand, a blood sugar well below 150 mg. per 100 ml. is not diagnostic of diabetes, and further investigation is necessary by the glucose-tolerance test.

Glucose-Tolerance Test

This test is more often used to exclude the diagnosis of diabetes mellitus than to establish its presence, for it is necessary only in those mild cases free from all symptoms of diabetes in which a single determination of the blood sugar gives an equivocal result.

It is essential to give the patient a full carbohydrate diet for seven days before carrying out this test. If not, a mildly diabetic type of curve may be found in a normal person.

After a full carbohydrate regime the patient is fasted overnight, blood and urine specimens are collected and analysed quantitatively and qualitatively for sugar before and half, one, one and a half, two, and two and a half hours after 50 g. of glucose dissolved in 200 ml. of water. The urine specimens should also be examined qualitatively for ketone bodies. In the normal curve the fasting blood sugar is below 110 mg. per 100 ml.; there is a rise to less than 180 mg. per 100 ml., and a return to the fasting level within two to two and a half hours. A second type of curve which is found in normal persons is the so-called lag storage curve in which the half-hour blood analysis shows an abnormally high concentration of sugar (up to 250 mg. per 100 ml.), but the specimens at one and a half and two hours have returned to the fasting level. Such a curve found in patients free from symptoms of diabetes is of no pathological significance and may account for the presence of sugar in the urine between half and one hour after a high carbohydrate meal, because of rapid absorption.

A normal curve is found in renal glycosuria, when sugar appears in the urine at times when the blood concentration is not abnormally high. Although renal glycosuria is usually of no pathological significance it should be borne in mind that the condition may be accompanied by other forms of renal tubular dysfunction causing amino-aciduria and, or alternatively, abnormal phosphorus excretion leading to persistent rickets. Such cases are rare, but the condition should be borne in mind when glycosuria without symptoms of diabetes is found in childhood. Indeed, all cases of glycosuria in childhood should be referred for diagnosis to a diabetic clinic.

The glucose-tolerance curve is abnormal and usually due to diabetes when the fasting blood sugar is above 110 mg. per 100 ml., the blood sugar rises to a level above 180 mg. per 100 ml. and fails to return to normal values within two to two and a half hours. However, abnormal curves may also be found in sepsis, carbohydrate starvation, hyperthyroidism, severe liver disease, Cushing's syndrome, and some cases of acromegaly, in all of which glycosuria may occur. Usually the non-diabetic causes of an abnormal glucose tolerance are obvious from the clinical findings and the abnormality is not very great.

Glycosuria and Hyperglycaemia in Known Diabetics

Glycosuria and hyperglycaemia must also be considered in relation to the known diabetic, possibly on insulin treatment, who is being controlled by the practitioner. The insulin requirements may be readily assessed by means of routine urine tests for glucose and ketone bodies, but occasional blood-sugar determinations are of value. The time at which the blood or urine should be collected depends upon the type and number of doses of insulin the patient is receiving. Sometimes an early morning specimen may be the best, sometimes the midday specimen, and in other circumstances both. It is not the purpose of this article to supplant the excellent manuals on the treatment of diabetes, but a few general principles may be useful.

While usually the presence of heavy glycosuria may be regarded as an indication for increasing insulin dosage, this is not always the case. The early morning specimen may contain sugar secreted into the bladder in the early part of the night after the evening meal. Clearly a urine test carried out on such a specimen will give no indication of the dangers of early morning hypoglycaemia. For this reason the bladder should be emptied immediately on waking and a further specimen of urine passed as soon as possible before breakfast. In this way the second specimen will be an indication of the fasting blood sugar; this specimen is the one most useful in controlling the dose of protamine-zinc insulin. Similarly it is better to test the second of two specimens passed before lunch or tea in cases on a morning dose of soluble insulin.

In cases on two doses of soluble insulin the morning specimen may be useless as a guide to dosage because the evening insulin may not act long enough to prevent morning glycosuria, but at the same time any increase in insulin dosage may produce hypoglycaemic attacks during the night.

Blood-sugar estimations make treatment easier but are not always essential. In diabetics with a normal threshold periods of hyperglycaemia will usually be accompanied by heavy glycosuria. Determination of the blood sugar in a diabetic patient receiving insulin treatment and not responding with clinical improvement may show that the patient still has a high blood sugar. On the whole, however, determinations of blood sugar in patients with known diabetes are of particular value in indicating hypoglycaemia and provide an indication for the reduction of the insulin dosage.

In any diabetic it is useful to know the renal threshold, because in patients with a low threshold insulin dosage cannot be adjusted by urine tests alone. Some reasonable control is possible if the insulin dosage is decreased when glycosuria disappears and increased when ketones appear in the urine. The threshold may be estimated by a series of analyses of sugar in the blood and urine. A convenient technique is as follows. Four hours after the morning injection of insulin the patient should empty his bladder. Ten minutes later the blood-sugar level should be determined, and as soon as possible after this, preferably within fifteen minutes, the bladder should be emptied again. No food must be taken from an hour before the first emptying of the bladder to completion of the test. The patient has a low renal threshold if more than slight traces of sugar appear in the second urine specimen and the blood-sugar level is below 160 mg. per 100 ml.

Collection and Preservation of Blood for Sugar Determination

Blood collected for analysis of its sugar content must be preserved with one drop of formalin or by the addition of potassium fluoride. It is best, however, to obtain prepared tubes from a local laboratory.

Most of the methods for determination of blood sugar are not entirely specific and the values are usually 15–25 mg. per 100 ml. higher than the true amounts. The figures for sugar concentration given in this article refer to capillary blood; it is important to remember that the content in venous blood is less than that in capillary blood. The difference is not great during fasting, but after a carbohydrate meal it may amount to as much as 20–70 mg. per 100 ml.

Next article on Clinical Pathology.—"Evidence of Gout," by Dr. Oswald Savage.

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CHANGES AND PROSPECTS IN MEDICINAL TREATMENT

SIR HENRY DALE'S HARBEN LECTURES

Sir Henry Dale, O.M., delivered the three Harben lectures, 1953, at the Royal Institute of Public Health and Hygiene on December 7, 8, and 9, taking as his subject, "Changes and Prospects in Medicinal Treatment." The chair was taken on the successive evenings by Sir Henry Tidy, Dr. J. Browning Alexander, and Sir Arthur MacNalty.

TREATMENT OF PRIMARY CAUSES, INFECTIONS, IMMUNOLOGY, AND CHEMOTHERAPY

In his first lecture Sir Henry Dale began a review of the remarkable changes which, during the past half-century, and largely in the recent quarter, have so transformed the whole aspect of medicinal treatment of disease that what was earlier recognized, by doctors and patients alike, as one of the more backward and ineffective aspects of medical activity had become one of the most successful and scientifically progressive. Medical men of his own generation hardly needed to be reminded of the days when "doctors' medicine" formed the target for a grim kind of humour. There was then a great disparity of aim and interest between the pharmacology of the laboratories and the therapeutic practice of the wards. What pharmacology had to say even about the action of the few unquestionably valuable drugs at that time had little reference to their therapeutic use. Paul Ehrlich complained of the pharmacologists of his time that if he asked them how quinine produced its effect they would tell him how it acted on the frog's muscle or on the mouse's brain, when what he wanted to know was how it specifically attacked the malaria parasites, causing them to disappear from the blood of a sufferer from malaria. What he wanted to know was how certain doses would cure the patient, not how large doses would poison him.

The lecturer illustrated some of the conditions which prevented the development of therapeutics as a science at a period well within living memory. He said that he mentioned these bygone anomalies and frustrations only to serve as a background for a discussion of the predominant factors which had brought about an astonishing change, a veritable transformation of the whole therapeutic outlook, in recent years.

The stimulus came largely from what at the time appeared to be an essentially new idea in therapeutics, the idea that a medicine should be used to remove or prevent the cause of a disease or a failure of health, whereas the most that had been previously expected of any medication was the relief or mitigation of symptoms, except perhaps in obvious cases, such as the removal of intestinal worms, where the cause of a disease had been readily visible to the naked eye. Of course, the relief of symptoms might still be the most immediate need for the patient and the most urgent duty of the physician. Nobody would depreciate the value of digitalis because it was essentially a remedy for symptoms, not an agent for the eradication of the cause of them, or because pharmacology might not yet have completed its account of the way in which the active constituents of digitalis produced their effects.

The Fertile 'Nineties

It was, however, to the conception of radical treatment of the primary causes of disease as the initiating stimulus in this new development that he would, in the first instance, ask special attention. The decade beginning with 1890 had a special significance in this respect. During that decade there were also profound discoveries in physics—the discoveries of Röntgen, Becquerel, J. J. Thomson, and Rutherford. The first two years of that decade saw the advent of three new lines of medicinal treatment, all concerned with the eradication, removal, or prevention of the primary causes of disease. These were the discovery by Emil von Behring of the diphtheria and tetanus antitoxins, Paul Ehrlich's first (though not practically successful) trial of chemotherapy, and George Murray's first successful treatment of a deficiency disease, myxoedema, by administering thyroid gland in myxoedema. From these separate seeds, in due course, were to develop the luxuriant growths of a progressive therapeutics based on immunology, chemotherapy, and endocrinology, respectively.

It would be possible, of course, to trace the ultimate origin of all immunological treatment to the inoculation against smallpox, practised originally in the middle of the eighteenth century, and more particularly to Jenner's vaccination introduced as that century was drawing to its close. But the last decade of the nineteenth century was surely the great fertile period. Sir Henry Dale devoted the remainder of the first lecture to a discussion of the two different types of remedial agent which deal directly with diseases due to infections by actions which stop the growth of the infecting organisms and lead to their elimination. These were the natural immunological remedies and the artificial chemotherapeutic agents, including the antibiotics.

Immunological Remedies

From 1892 onwards inoculation with killed cultures of bacilli was undertaken for protection against cholera and later against plague. Afterwards came Almroth Wright's similar immunization against typhoid, effective in the first world war; and then the active inoculations against diphtheria and tetanus. Many years were likely to pass, however, before the antitoxins could be spared from the list of essential remedies; perhaps they never would be spared.

Further advances in the effectiveness of both methods of conferring immunity, active and passive, against bacterial infection seemed most likely to come from a deeper know-

ledge of the chemistry of the antigenic constituents of bacteria and their toxins. Again the first impulse to inquire into this field came from Ehrlich's well-known side-chain theory, which gave a quasi-diagrammatic but essentially a chemical conception of the relation between antigen and antibody. Most recent conceptions did little more than restate the essential idea of Ehrlich in more modern terms, with the aid of such new chemical knowledge and conceptions as Ehrlich himself would have been eager to incorporate in his theory. Such a theory, in any case, had its chief value as a scaffold for ideas, making it possible to build a new exploratory extension of the fabric of experimental research.

Chemotherapy

Already in 1891 Ehrlich was intent on the possibility of discovering new artificial compounds which would have a maximum affinity for the toxic agent or parasite with a minimal affinity for the organs of the infected animal or human being. He was trying methylene blue because it visibly stained the malaria parasite under the microscope; and, tried on the human being, it had a certain therapeutic action, though not as good as that of quinine. The first early promise of successful chemotherapy appeared in 1903, at a time, said Sir Henry Dale, when he himself happened to be working in Ehrlich's laboratory. Ehrlich and Shiga had then already discovered trypan red, which would cure a trypanosome infection in mice. From this starting-point came progress, eventually, to suramin (germanin). From another (atoxyl), development led to salvarsan, as the earliest major practical triumph of chemotherapy. In recent years other effective agents, including several antimalarials, had appeared.

In 1935 came the introduction of prontosil, and then its active moiety sulphanilamide and the various derivatives; and while this development was still proceeding Florey and his co-workers, in 1939, re-examined the possibility of producing and purifying, on a scale adequate for systematic clinical trials, Fleming's penicillin; and the curative action of penicillin had been found to extend far beyond the contemplated range of bacterial infections. It had, for example, provided an additional remedy for syphilis, so safe and effective that even the importance of salvarsan had receded. After this came the first claims of the new range of other antibiotics—streptomycin, and chloramphenicol, with a chemical structure of unexpected simplicity, and many others. There seemed to be a prospect now of an indefinite series of antibiotic agents, many of the more recent of which showed a similarity in what might be called the "spectra" of their antibiotic actions; so that it might be supposed that such a series of equivalents was embarrassing rather than useful, but that would be a hasty judgment. The development of resistant strains might give special value to a range of alternatives.

In summing up, Sir Henry Dale said that all the evidence appeared to favour the conception of successful chemotherapy as normally due to a relatively long-persistent action, involving a corresponding maintenance of effective concentration of the remedial agent in the blood—a war of attrition rather than a *Blitzkrieg*. The general type of action, at the levels of concentration normally obtainable in actual treatment, was to suppress the further multiplication of the infecting organisms rather than to kill them outright. The whole tendency of some recent evidence favoured the view that this chemotherapeutic effect was produced by rendering unavailable to the parasitic organism some essential nutrients, which its nuclear apparatus specifically required for the purpose of its normal multiplication.

He thought the rapid advance in recent years of such an intimate cellular biochemistry was likely to provide a basis for interpretation which Ehrlich would have rejoiced to adopt in place of his more diagrammatic conception. But the initiative was due to the brilliant imagination and determined scientific enterprise of Ehrlich, the centenary of whose birth was to be celebrated a few months hence, on March 14, 1954; and, by a coincidence, the following day, March 15, was the centenary of the birth of Emil von Behring, the discoverer of the diphtheria and tetanus antitoxins.

HORMONES

In his second lecture Sir Henry Dale spoke first of deficiency diseases, including conditions due to endocrine and vitamin deficiencies, in which the treatment, once the nature of the condition had been recognized, was the obvious one of replacement by administration of what was missing. Murray's treatment of myxoedema was the first example of the success of a replacement therapy. After this there was a long interval, during which, though there were discoveries in endocrinology, most of these had no direct applications to treatment by replacement. One exception concerned the rather rare condition of *diabetes insipidus*, due to a deficiency of the pituitary posterior lobe, in some cases following, perhaps, injury in the neighbouring hypothalamus—a condition which could be made good by injection of post-pituitary extract. He did not know even yet whether the new synthetic pressor principle would also have an antidiuretic action.

He had a vivid memory of the days of disillusionment and doubt among research workers, with regard to the practical possibility of any further successes on these lines. There was at that time no warrant for assuming, from the experience thus far available, that other hormones, even if they existed, would be accumulated in other endocrine glands in such quantities as to be obtainable from them by extraction. They might, on the other hand, be so unstable in their chemical properties, that they would inevitably be lost in any method applied for their extraction. Uncertainties of this kind, and the knowledge of the failure of so many attempts, had a strong deterrent effect until there came the discovery in 1921, by Banting and Best, two young and inexperienced Canadians, who found that the diabetic hormone of the pancreatic islets could actually be extracted, and produce its remedial effects when artificially injected. This provided a new starting-point for active and progressive research in a much wider field of endocrinology.

It would be superfluous on his part to elaborate the importance of insulin in the treatment of diabetes, and its revolutionary effect so far as the sufferers from that disease were concerned. It seemed, however, that the discovery of insulin had had an effect of much greater importance in making possible other discoveries. It led to a new spirit of optimism and enterprise. The sealed book was opening at last, and the subsequent years saw further chapters disclosed. The concurrent advance in the methods of organic chemistry had been important factors in accelerating this progress. But there had been a two-way traffic, and the rapid widening of this new prospect in endocrinology had served as a powerful stimulus to the necessary advances in biological and organic chemistry. Diseases due to other hormone deficiencies came in succession under treatment by direct replacement, and a long series of steroid hormones from the gonads and the suprarenal cortex had been isolated, and later made by artificial synthesis. This series afforded a striking example of the manner in which endocrine functions, differentiated and described in physiological terms, had been clearly associated with steroid chemical structures differing in detail, but still bearing a very close relationship in their general plan.

The qualified expert could easily take a whole course of lectures for the presentation in detail of this subject alone. Another such course might be devoted to the story of the astonishing series of functionally different hormones which had been successfully recognized as existing within the small compass of the anterior pituitary lobe. Each of these hormones had some separate function. Up to 1934 claims had been put forward by different investigators for the recognition of some nine different hormones in this one very small anterior pituitary lobe, though he did not think it could be regarded as quite certain that all of those so described were different. And the question was not made easier by some recent observations by Best and his present co-workers showing that, when the pituitary body had been removed from rats, insulin itself would act as a growth-promoting hormone in the sense that regular injection evoked a renewal of the normal growth.

He thought it should be noted, before leaving this aspect of the general subject, that the instances of a completely successful treatment of a hormonal defect, by direct replacement of what was missing, were still not numerous. The thyroid gland and its constituents in myxoedema, posterior lobe extract in *diabetes insipidus*, and insulin in *diabetes mellitus* were still the outstanding examples, though many successes of a lesser kind could of course be claimed.

Another point to which he wished to draw attention, concerning the therapeutic use of hormones, was that physicians, in more than one important instance, were employing these or their artificial analogues, not to replace defects in the ordinary sense, but to produce their physiological actions at intensities above the normal, physiological range. This was true of the use of oestrogenic hormones, or the analogous stilboestrol, to restrain the growth of prostatic cancer in the male, and testosterone to restrain the growth of mammary cancer in the female. A more conspicuous example was the use of cortisone and A.C.T.H. to allay pain and swelling in the joints in rheumatoid arthritis; and he asked his audience to note that these uses of hormones, for purposes other than the repair of hormonal deficiencies, provided a bridge between the treatment of causes and the treatment of symptoms.

Vitamins

Sir Henry Dale turned next to the accessory nutritional factors or vitamins. This was far more ancient history. The antiscorbutic value of fresh fruits and vegetables had been discovered, forgotten, and rediscovered almost in each century from the sixteenth onwards. Even during the first world war support was still being given on high authority to the idea that scurvy was due to acidity or reduced alkalinity of the blood. The value of cod-liver oil in rickets was discovered in 1840, but even after the first world war rickets remained a pathetically frequent malady amongst children in industrial areas. Then came the work of Mellanby on rickets, which, with the earlier researches of Hopkins and others on the more general significance of such dietary deficiencies, initiated an amazingly rapid advance of knowledge in this field.

Looking back, one found it difficult to believe that even for some years after the first world war the belief was still current that vitamins were substances present in such minute proportions in such complex mixtures, and probably so unstable, that it was quite doubtful whether any of them would ever be isolated or made otherwise accessible to detailed chemical examination. But between 1926 and 1939 at least 10 vitamins had been isolated, identified, and made artificially. Here again, as in the case of the hormones, this progress, when it once began, was astonishingly rapid.

Antihistamines

After glancing at the claims and uses of the various vitamins as practical remedies, Sir Henry Dale devoted the remaining section of this lecture to the introduction in recent years of the antihistaminic series of remedies. This illustrated what appeared to him to be, possibly, a new phase in therapeutic enterprise—the discovery of remedies preventing the action of a substance—histamine in this case—which had been recognized as the common, proximate cause of the symptoms of a group of diseases and pathological syndromes.

SUBSTANCES MODIFYING THE TRANSMISSION OF NERVOUS EFFECTS

In his closing lecture, before proceeding to some general conclusions, Sir Henry Dale discussed another example of recent advance based upon new and still progressive knowledge of the chemical changes concerned in the natural reactions of the body. This dealt with the activities and therapeutic possibilities of substances, both natural and artificial, which modified the actions of chemical transmitters of nervous effects at synaptic junctions. It had been known for nearly 40 years that acetylcholine had stimulating actions, not only on the plain muscle and gland cells responding to autonomic nerve impulses, but also on the nerve cells of the peripheral ganglia and on the motor end-plates of voluntary muscle fibres; and that these latter actions were susceptible to the paralysing effects of curare and of excess of the primarily stimulant nicotine.

Until a few years ago curarine and its substitutes were chiefly of interest as pharmacological curiosities and as technical aids in physiological experiment. It was only in recent years that the true meaning of curarine action was discovered and shown to be essentially a suppression of the normal sensitiveness of the end-plates to acetylcholine. This, together with the isolation of a pure tubocurarine by H. King, had made it possible to use curarine for the production of a paralysis of the voluntary musculature, as a supplement to anaesthesia in operative surgery.

He entered upon a detailed discussion of the paralysing and transmission-blocking agents at the neuromuscular and ganglionic synapses, and referred in particular to the paper in the *British Medical Journal* of December 5 (p. 1237) on the use of an artificial hypothermia in conjunction with autonomic block and paralysis of voluntary muscles.

RETROSPECT AND PROSPECT

In concluding his lectures Sir Henry Dale spoke in somewhat wider terms of the progress of 50 years. After saying that not so many years ago he would have recoiled from the rashness of the forecast he had been making, he went on:

> "I have seen so many cases, one after another, in which pessimism with regard to therapeutic possibilities has been suddenly put to shame by a courageous initiative. I have seen so many diseases, long regarded as beyond any reasonable hope of cure or relief, brought within the range of a medicinal treatment which has dealt with the primary cause directly, eradicating it or showing the way to prevent its occurrence, and thus banishing the disease from a whole community, or rendering it relatively innocuous. And I have seen these things happen so many times, and have been watching their frequency gather speed so continuously now for more than half a century, that, so far from finding myself subject to the disillusionment proper to my age, I feel bound to regard an attitude of hopeful, even of confident expectation concerning further developments in this direction, as not merely excusable, but as the only attitude which can be scientifically justified."

He went on to speak of the impressions left on his memory of the therapeutics of his student days at the turn of the century. His main impression was the lack of any effective medicinal remedies for almost all the serious illnesses, acute and chronic, which came to hospital for treatment—cases of diabetes mellitus, of pernicious anaemia, for example, admitted for observation or as subjects for teaching, without any hope of anything effective in the way of treatment, except, as one physician said, "to prolong the poor fellow's life by making the rest of it not worth living." In rickets there was at the time of which he was speaking a sound empirical observation waiting to be applied, but only fanciful aetiologies and treatments, till research showed the way much later. Diphtheria was the only infectious disease for which a specific treatment was then available. For the other acute infections—pneumonia, meningitis, erysipelas, septicaemias, or the common infections of childhood, none was yet in prospect. For none of these could anything be really done except to isolate the patient when necessary for protection of the community, and to keep him reasonably warm and quiet, and to administer anything likely to give him rest and keep up his strength. For the rest, the *vis medicatrix naturae*. Such therapeutic innovations as the newer types of remedies dealing with the proximate causes of symptoms were still far below any visible horizon. Only here and there were there any signs of the great change which was soon to begin; there was still but little general and positive advance from resources and methods which had been available 50 years earlier. The former drastic purgings and bleedings had been discarded, but there was little in the way of fresh therapeutic enterprise, and the prevailing mood was one of a placid acceptance, or of a cynical scepticism.

They had seen how all that had changed. Salvarsan, insulin, thyroxine, sulphanilamide, penicillin, the steroid hor-

mone, the antihistamines—these and others he had mentioned as examples of the way in which therapeutics was now progressing.

Further Advances

What further advances were in prospect? An observer of the general situation would have the hope, if not the confident expectation, of further important advances in the curative or, better, the preventive treatment of the common virus infections. Anybody unacquainted with the technical difficulties might reasonably inquire why, after more than 150 years, we had not any method of preventive inoculation, comparable with Jennerian vaccination against smallpox, for most of the still common virus infections of our temperate zone. The real trouble was that hitherto the viruses which people had succeeded in cultivating outside the body happened, unfortunately, to be those like influenza for which no solid immunity was acquired, even from an attack. It could only be said that there was so much accumulated experience and trained ingenuity now employed on relevant researches that it ought not to be long before there was discovered a generally applicable preventive inoculation against one or more of the diseases of this group, or perhaps an effective treatment by some antibiotic or other remedy.

What was going to be done with all this new knowledge? The position had been transformed, as compared with that of only 20 years ago. The change had been, on balance, enormously for the better. The question was bound to arise, concerning the limits of the individual intelligence to absorb, to understand, and to apply all this swelling flood of genuine and potentially useful new knowledge. He had been conscious, during this lecture, when speaking of the intricacies of the different types of paralysing and transmission-blocking agents at neuromuscular and ganglionic synapses, of his own difficulty in expounding, even of being certain that he himself understood completely some of these developments, although they were related to a range of physiology which had been that of his own special interest and concern. And he had wondered how the student of medicine was to be brought into contact with these things, and so to absorb them as to use them safely and intelligently in his practice.

This kind of educational problem, due to the increasing range and complexity of knowledge, was common, of course, to all branches of the medical discipline, and indeed to the learning of all the natural sciences; though it might be suspected that it was unusually acute in medicinal therapeutics on account of the rapid extension there from such small beginnings to this embarrassing abundance. Yet, here as elsewhere, the problem had somehow to be solved. He had himself long felt a strong conviction that the central aim of any scheme for a national health service ought to have been—ought still to be—to deal with this problem, of providing such technical facilities and assistance, such ease and regularity of access to expert advice and consultation, as would enable the individual practitioner to bring the highest practicable proportion of all this new knowledge that research is now producing, and would continue to produce, to the service of his patients, in the diagnosis and treatment of their ailments, with all the help that science could progressively offer.

THE DOCTORS' DISEASES

Addressing his fellow actuaries recently, Mr. E. A. J. HEATH, manager of the Medical Sickness, Annuity, and Life Assurance Society, was concerned mainly with the problems of "permanent" or "non-cancellable" (that is, by the Society) insurance for sickness. But he had also much of interest to tell about the cause of sickness among the members, most of whom are men doctors. Comparing two peacetime years, 1937 and 1952, there was actually a reduction in the rate of claims for benefit owing to the occurrence of an influenza epidemic in the former year but not in the latter. Still, it was reassuring to hear that, unlike some industrial experience, there had been no general increase. Within this picture there were remarkable changes, however, that mirrored some of the recent trends of morbidity in the general population. Claims for septic infections were three times commoner in 1937 than in 1952; there were no claims for scarlet fever or diphtheria in the later year. Appendicitis was only half as common in 1952, and why this should be so was not at all clear. Surprisingly, pneumonia seemed to be commoner in 1952, though disability was probably much shorter, and as a cause of death pneumonia was now "practically non-existent." The speaker was dealing, of course, with a membership that ceases at 65 years of age.

A Fashionable Complaint

The other side of the balance sheet showed an increase in the claims for an assortment of conditions—for virus infections, for "disks," possibly for cancer, and, dominating the picture, for coronary thrombosis. This is what Mr. Heath had to say about "disks":

"In 1937 there were 47 claims for lumbago, sciatica, sacro-iliac strain, and so on, on the average of fairly short duration. In 1952 there were only 29 such cases—but no fewer than 35 cases of prolapsed intervertebral disks, with a definite increase in the average period of incapacity. I am told that prolapsed disks have been found in skeletons 2,000 years old, but they have only been rediscovered since the war, and very much to the cost of companies doing sickness insurance. Fortunately the drastic operation which was in vogue a few years ago has already fallen out of favour and disks tend more and more to be treated conservatively." It is not often that fashions in diagnosis—and treatment—are documented so neatly.

Coronary Thrombosis

The increase in coronary disease may be represented by these numbers: 9 claims in 1937, including 1 for angina pectoris, and 24 claims in 1952, including 4 for angina. (The figures given for 1952 were all "adjusted" figures, to allow for the changes in the number of members between 1937 and 1952 and the increase in the average age of the members.) Scrutiny of the other cardiovascular claims in 1937, and review of all the other information on the subsequent history of the claimants now available yielded another 6 cases in that year that might conceivably have been "missed coronaries." This procedure (which was not applied to 1952) permits a more conservative comparison of 15 claims in 1937 with 24 in 1952—similar figures to those of the deaths from coronary disease, 6 and 9 respectively. In addition there were 3 "chronic" cases of coronary thrombosis in 1937 and 8 in 1952. On the other hand, there was no apparent increase in these 15 years in the claims for intracranial vascular disease and high blood pressure.

Mr. Heath summed up the outlook in coronary thrombosis as "roughly speaking, one-third die within a day or two, one-third recover in 3 months, and one-third are incapacitated for 6 months or even for many years"—figures not unlike the results of the exhaustive analysis of prognosis in the same material reported previously in our columns.[1] Coronary thrombosis, he said, was probably "the biggest medical problem which life office actuaries have to face today, and it is even more important in the sickness field," which is not surprising in light of the observation of Morris and his colleagues that one in five members joining the society at the usual age may expect to suffer from coronary heart disease before reaching 65, and that a third of all the deaths are so caused.

[1] Morris, J. N., Heady, J. A., and Barley, R. G. (1952). *British Medical Journal*, 1, 508.

Reports of Societies

USE AND ABUSE OF REST

On November 24 at the Royal Society of Medicine the Section of Medicine, with the president, Sir HENRY COHEN, in the chair, held a discussion on the use and abuse of rest as a therapeutic measure. In opening the discussion Dr. G. E. BEAUMONT extolled the value of rest in medicine. Although there was a modern tendency to emphasize rest for the mind as well as the body, it was remarkable how quickly a patient became indifferent to his worries when he took to bed with an acute illness. Even more remarkable was the mental tranquillity so often seen in chronic illness: indeed, the patient with an empty mind, who adjusted himself easily to prolonged rest, often derived most physical benefit from treatment. Patients in hospital were sometimes disturbed by visitors, visiting-hour often being followed by a rise in the patient's temperature.

Physical rest was of paramount importance in the early treatment of poliomyelitis. In pulmonary tuberculosis, many of the results obtained by prolonged bed rest in the old days compared favourably with the achievements nowadays attributed to chemotherapy. Treatment by pneumothorax or thoracoplasty was an adjunct to rest, but the physical exercises which had become part of the treatment in patients with pulmonary tuberculosis subjected to pulmonary resection were contrary to the basic principles of treating tuberculosis, and might activate latent foci in the opposite lung. Sciatica had once been treated vigorously though unsuccessfully by physiotherapy, but now it was suggested that prolapse of the intervertebral disk was the true cause of sciatica, and so patients were being successfully treated by rest. In rheumatoid arthritis treatment by complete bed rest for many months was better than subjecting the patient to the rigours of physiotherapy and spa treatment. It should be the physician's aim to treat fewer patients more thoroughly.

The Hazards of Rest

Professor W. MELVILLE ARNOTT emphasized the abuse of rest in treatment. Rest was often loosely applied to mean periods of relief from work. The erroneous belief that hard work caused disease was readily accepted by doctors who were reluctant to admit their ignorance about the cause of disease and by patients who avidly welcomed such a palatable explanation of their woes. The main drawback to rest was that it could be definitely harmful. Rest was a "drug of addiction," but unlike other such agents its prescription was untrammelled by law. It was traditional to rest sick people, but proof of its value was lacking. When young people were put to rest many adverse metabolic and circulatory changes could be demonstrated. In elderly patients the hazards were even greater. It was common knowledge that incontinence in the aged could often be cured by the simple expedient of getting the patient out of bed, and alimentary function improved when a bedside commode was substituted for the bed-pan. It was remarkable that bed rest was seriously considered as a therapeutic measure, since its use was not even backed by tradition. Rest was a habit which had arisen from the principles of Hilton's *On Rest and Pain* and which had been perpetuated by the influence of the hospitals where the bed-pan routine and thoroughness of nursing had encouraged treatment in bed. An excess of rest, like an excess of drugs, was a burden on the Welfare State.

The Surgical Patient

Professor C. A. WELLS thought that many of the principles underlying treatment by rest were out of date, since we were now able to alter the course of so many diseases by modern therapy. It was essential to distinguish between the need for local rest for a diseased organ and general rest for the whole body. The symptom of pain could sometimes be treated by active means, as in the treatment of angina of effort by sympathectomy. Nowadays the main value of institutional treatment in pulmonary tuberculosis was to ensure that a complicated regime of chemotherapy was carried out, but the principles of resting diseased joints remained unchanged. A combination of rest and exercise was often the most successful way of treating orthopaedic disorders. In the field of general surgery early post-operative activity and ambulation had greatly reduced the risk of thrombo-embolic complications.

The newest approach to rest therapy was the process known as hibernation. By paralysing the heat-regulating mechanism and by cooling the body it was possible to produce a state of profound depression in which oxygen consumption was lowered without risk of cerebral or cardiovascular damage. In this state of almost completely suspended animation it was possible to carry out surgical operations while minimizing the risk of surgical shock and abolishing many of the harmful post-operative metabolic disturbances.

Rehabilitation

Group-Captain C. J. S. O'MALLEY discussed the place of rehabilitation in the treatment of disease. The need for rest in some diseases had decreased since the introduction of antibiotics. Although rest was still required in the acute phases of a disease, it was often found during rehabilitation that much effort was needed to overcome the apathy and ennui arising from too much rest. In rehabilitation centres it was vital to strike a careful balance between rest and activity. The timing of treatment was also important, especially in poliomyelitis, where complete rest was needed in the early stages. Active rehabilitation had reduced the length of disability after surgical operations in men on active service and in factory workers. During rehabilitation periods of relaxation were necessary: remedial games and work therapy helped to balance work with leisure. In many diseases, such as prolapsed intervertebral disk and osteoarthritis, exercises aimed at maintaining good muscle tone were most valuable. Patients with psychoneurotic disorders often responded well to rehabilitation, especially if they could be brought into contact with patients recovering from severe organic disabilities. Treatment in an active rehabilitation unit not only accelerated a good functional recovery but it was much more economical than prolonged treatment in hospital.

Nova et Vetera

TALES OF A POMANDER

The Gold-headed Cane. By William Macmichael, M.D. Seventh edition with foreword by James J. Waring, M.D., and preface by William J. Kerr, M.D. Containing the text and illustrations of the fifth edition, including the introduction by George C. Peachey. (Pp. 185; illustrated £2 7s. 6d.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1953.

The title of this most readable of books on medical history may need explanation. Even within living memory the costume of doctors was almost as distinctive as that of the clergy. For centuries before that, part of their equipment was a long cane, the spherical head of which was a "pomander" and contained sweet-smelling herbs, thought to be preservative against infection. The pomander itself died out in the seventeenth century, but until the end of the eighteenth the doctor was distinguished by his elaborate and expensive stick. Such a cane was owned by John Radcliffe (1650–1714), most successful and least literate of the great doctors of the age, who, owning no books and reading none, left a fortune to endow a library. From him the cane passed successively to Richard Mead (1673–1754), Anthony Askew (1722–1774), William and David Pitcairn, uncle and nephew (1711–1791 and 1749–1809), and Matthew

Baillie (1761–1823). None except the last made any important contributions to medical science, but all in their day were famous and successful physicians, undoubtedly alleviated much suffering, and accumulated what seem to-day incredible sums from their practices. All were shrewd, far-seeing, kindly men of great personal prestige and peculiarly resourceful in relieving symptoms. Which of us in sickness would not wish to be attended by such a one?

It is the peculiar skill of the author of this work, William Macmichael (1784–1839), that he brings all this home to the reader. The method of endowing an inanimate object with the power to relate its experiences has been often tried, and by several good writers. With this one exception the result has always been failure. Macmichael alone, so far as the reviewer's knowledge extends, has been triumphantly successful in his handling of this clumsy and rigid device, and the book fully deserves its popularity. The first edition of it appeared in 1827; this, the seventh, has a preface by Professor J. J. Waring, director of the tuberculosis institute of the University of Colorado, and an introduction by Professor W. J. Kerr, of the University of California, together with the learned and amusing essay on the book by the late Dr. G. C. Peachey. It is by far the most beautiful of the seven editions, each of which is itself a bibliophile's piece. The ancient cane rests at the Royal College of Physicians of London. It is entertaining to learn that a replica of it is now awarded as a prize at San Francisco:

"To sounds that echo further West
Than its sire's Islands of the Blest."

CHARLES SINGER.

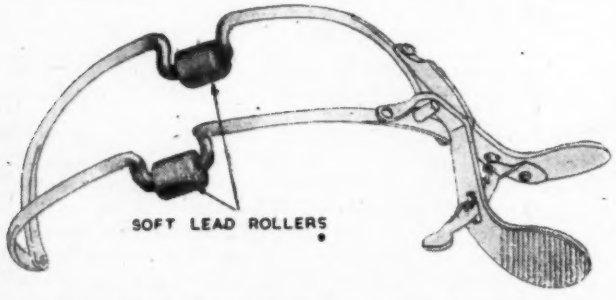
Preparations and Appliances

A MODIFIED WHITEHEAD GAG

Dr. A. OWEN-FLOOD, consulting anaesthetist, Hornsey Central Hospital, writes: Deciduous teeth extracted by means of a mouth gag during tonsillectomy can give the surgeon and anaesthetist cause for concern. The anaesthetic, of necessity deep enough for insertion of the gag, must at the same time allow a prompt return of the reflexes, and is thus, at the best, of a swinging type with a fairly stiff jaw.

The three danger points are: inserting the gag; the liability, when using the adenoid curette, of undue pressure on the front teeth; and taking out the gag with the jaw stiffening.

To a Whitehead gag, ideal for the partially toothless, giving an even pressure all round the jaw, I have fitted soft lead rollers where the gag is supposed to fit behind the front teeth (see illustration). This device makes insertion



of the gag simple and atraumatic, acts as a buffer against the shaft of the curette, and facilitates removal with a jaw beginning to tighten.

Any handy hospital engineer can fit these rollers, which are jointless, but care must be taken that they will not become loose and fall into the mouth. It is essential that they should be applied in a strip and be thick, so that on being bitten they do not alter their shape and thus cease to roll.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Carcinoma of the Female Breast

SIR,—Mr. David Patey's recent letter (*Journal*, November 7, p. 1046) raises a number of interesting points in connexion with our article on carcinoma of the female breast (*Journal*, October 10, p. 787).

The question of how effectively irradiation can destroy cancer in the axillary and internal mammary glands is a difficult one to answer and we, of course, did not investigate this directly. Elsewhere, one of us has jointly[1] reported the results of histological investigation in a series of irradiated tumours and we would agree that irradiation does fail to sterilize the glands in a fair number of cases. It is, however, extremely difficult to decide about the viability of cells in histological sections. In so far as our recent series can give an indirect answer to this question, it seems possible that incomplete sterilization of the axilla is unimportant in a majority of cases, since so many of these already have more distant spread. However, a patient with a solitary deposit in a low axillary gland and no distant metastases should be better off with that gland removed. There can be no doubt that such cases are few in number, that clinical assessment can be most misleading, and that there is no way of recognizing them prior to operation and full pathological investigation. If we could confidently recognize these cases, then, notwithstanding the greater morbidity, it would be logical to do a radical mastectomy in order to offer them the best chance of survival and the least chance of local recurrence. We would largely agree with Mr. Hedley Atkins's view, reported in your leading article (*Journal*, October 10, p. 817), that in terms of survival it is likely that in a small fraction of cases only does the method of treatment really matter. In terms of morbidity, however, the method of treatment does matter to a much larger number of women.

Mr. Patey has also raised an important point about the technique of simple mastectomy. It is true that some of the axillary glands are bound to be removed if the axillary tail of the breast is properly dissected, and Mr. Patey is right in saying that it is a question whether axillary dissection should be complete or limited.

In turning to the subject of the internal mammary glands, Mr. Patey writes that we "appear to assume that irradiation of the internal mammary chain is efficient." We have no evidence on this point, but it is likely that irradiation of these glands is no more and no less efficient than of those in the axilla. It is likely, however, that the number of cases in which super-radical surgery can effect survival is very small, and once again we have no means of predicting these cases beforehand. If we are to do the greatest good to the greatest number it would seem likely that super-radical surgery is unjustifiable. We stand corrected if we seem to have condemned this method without trial, but we do submit that such signs as there are point strongly against any more heroic surgery. If the experiment is to be continued we would plead that it should be a carefully controlled one from the outset. The radical operation was accepted for many years without any proof of its value, and it would be regrettable if it took as many years and the suffering of many women to prove that super-radical surgery is unjustifiable as well as mutilating.

We are glad that Mr. Patey has questioned our local recurrence index. As stated in our paper, the method was put forward in order to stimulate comment and criticism. In a retrospective survey, such as we presented, it was very difficult to collect adequate and accurate information on many points. The simple surgery group included many cases which were treated by very limited local surgery and our numbers did not allow more detailed analysis. The local recurrences included a wide variety of circumstances—for example, a fresh or recurrent tumour in a case treated by local excision only, and recurrences in the skin or chest wall following mastectomy, as well as recurrences in the undissected and dissected axilla. If further investigation reveals that local recurrence is less common after radical than after adequate simple mastectomy (and we would emphasize the word adequate, since the latter operation is sometimes carelessly performed),

then this will be an important point in favour of radical surgery. It may be that in the past too much emphasis has been placed on survival figures and too little on morbidity and local recurrence. If two hypothetical and identical cases, A and B, are considered, the one treated by radical and the other by conservative surgery, it may eventually prove true that case A has the greater chance of a swollen arm, and case B the greater likelihood of local recurrence. If both cases survive for the same time it becomes extremely difficult to assess the merits and disadvantages of the two methods of treatment.

Though our own advocacy of conservative surgery may be partly demolished in the process, we would earnestly ask all workers to give very careful attention to this problem of local recurrence. In the meantime it is our considered opinion that, in the absence of any more exact method for really accurate pre-operative assessment of our cases, the greatest good and the least harm will be done to the largest number if less radical surgical methods together with radiotherapy are used in the great majority of cases.—We are, etc.,

R. S. MURLEY.
I. G. WILLIAMS.

Radlett, Herts.

REFERENCE

1 Williams, I. G., and Cunningham, G. J. (1951). *Brit. J. Radiol.*, **24**, 123.

Malaria in Neighbouring Londoners

SIR,—The article by Drs. G. S. Crockett and K. Simpson (*Journal*, November 21, p. 1141) was of considerable interest to me. In 1950, with the co-operation of Mr. A. W. Leftwich, biology master, and the boys of the Wellingborough Grammar School, I carried out a survey of the different species of mosquitoes in the area. This area, which is a rectangle bounded by National Grid Lines E4/83 to E4/98 and N2/64 to N2/70, covers about 50,485 acres and includes the junction of the rivers Ise and Nene. The total number of specimens examined by us was 557, and of these 20 were of anopheline mosquitoes. The anopheline variety was *Anopheles maculipennis* and its subdivisions. Although the survey was far from being complete, it did show that the anopheline mosquito was no rarity in the district.

I appreciate the difficulty experienced by the writers of the article in finding the breeding ground of the anopheline mosquito, as we, too, experienced difficulty. We found the anopheline breeding in shallow reed-grown pools of overflow water from the river Nene. We also found some breeding in a water tank situated on the outskirts of a small town. The breeding grounds of the *Culex* variety were found much more easily. Adult anopheline were found to range one to two miles from their breeding grounds, and of course, if a swarm were caught by a wind, could be transported much further distances. This article brings to mind that, with air transport and persons returning from malarious countries, given a certain period of warm weather for the malarial cycle to be completed, there is always the potential danger of primary malaria being contracted in England.

As a matter of interest, of the 30 or more known British species of mosquito, only six were found in this district. The species and numbers of specimens were as follows: *Theobaldia annulata*, 14; *Theobaldia (culicella) morsitans*, 18; *Aedes (ochlerotatus) rusticus*, 27; *Aedes cantans* (formerly *ochlerotatus waterhousei*), 33; *Culex pipiens*, 445; *Anopheles*, 20. It is interesting to note that 60 specimens of *Aedes rusticus* and *Aedes cantans* were found. These specimens are related to the *Aedes aegyptus*, which is associated in Africa with the spread of yellow fever.

Considering the fact that mosquitoes are associated with the spread of diseases in tropical countries, one wonders if they could be the possible vectors of certain diseases in this country.—I am, etc.,

P. X. BERMINGHAM.

Wellingborough.

Costo-clavicular Compression of the Subclavian Vein

SIR,—I read with interest the article by Dr. R. Wyburn-Mason under the above title (*Journal*, November 28, p. 1198). It is true that in recent years the conception of costo-clavicular compression of the brachial plexus has been recognized as often giving rise to symptoms formerly attributed to the pressure of a cervical rib or to compression by the scalenus anterior muscle. Unfortunately, the impression that lesions causing dropping or drooping of the shoulder produce costo-clavicular compression of the neurovascular bundle is still widely held. It is a fact well known to all anatomy students that when the shoulder descends the clavicle moves anteriorly away from the first rib. The further the shoulder descends the wider does the costo-clavicular interval become. Conversely, when the shoulder is raised, as by abducting the arm or retracting (bracing back) the shoulder, the clavicle moves upwards and backwards in the form of an arc, and the costo-clavicular interval becomes narrower.

The relationship of clavicular movements to costo-clavicular compression was pointed out by Professor E. D. Telford and myself in the *Journal* of March 15, 1947 (p. 325). The production of pain due to dropping of the point of the shoulder is caused by a dragging of the plexus across the tendinous anterior edge of the scalenus medius. Oedema is caused by a similar drag of the vein over the first rib, as shown by Dr. Wyburn-Mason. I quote the comment following the first two case reports in Dr. Wyburn-Mason's article: "It appears, therefore, that when the tip of the shoulder drops because of damage to or tearing of structures normally supporting it the subclavian vein may be compressed as it passes over the first rib, giving rise to venous oedema of the arm." It is significant that the author does not say ". . . compressed *by the clavicle* as it passes . . . ", and from this comment I think that he does not believe that the clavicle is an agent in this venous compression. The more unfortunate is it, therefore, that costo-clavicular compression is the title of this article.—I am, etc.,

S. MOTTERSHEAD.

Middlesbrough

Venepuncture

SIR,—In his article on venepuncture (*Journal*, October 24, p. 930), Dr. I. A. B. Cathie recommends the patient bending the elbow double tightly over the swab after the removal of the needle from the vein. I do not think that this common practice is the best. Not only does it dam blood back in the forearm, but it may also make a short, tight sleeve on a female patient into an effective tourniquet around the contracting arm muscles. In either case a propensity to bruising and bleeding is increased. It seems far better to leave the elbow extended and press the swab with the whole arm slightly raised. This is no more trouble than the usual method, and mishaps are less common.—I am, etc.,

P. J. TAYLOR.

Liverpool.

Fatality Following Penicillin Injection

SIR,—It seems desirable in the present state of our knowledge that every fatality following a penicillin injection should be given wide publicity. Here is another fatal case.

An apparently healthy woman, aged 31, who two years previously had been successfully treated in this hospital for phlebitis of the right leg (of unknown origin) with 53 injections of crystalline penicillin, was readmitted on September 21, 1953, for the removal of a chronic appendix. On the morning after admission she was prepared for operation, but on being given the routine pre-operative injection of morphine and atropine she passed into shock, and though she made a perfect recovery the operation was postponed for further examination of her general condition. Four days later, as nothing abnormal had been discovered, she was once more prepared for operation, but it was decided to omit the injection of morphine and atropine. A chronic appendix was removed under cinchocaine spinal anaesthesia (isotonic) and the patient left the theatre in apparently perfect condition, having had no fall of blood pressure or other untoward incident. One and three-quarter hours after being returned to the wards the patient received 50,000 units of crystalline penicillin into the buttock, and immediately, announcing that she was going to die, became cyanosed and pulseless. She succumbed 15 minutes later in spite of artificial respiration with oxygen, injections of nikethamide, caffeine, ouabain, and, finally, adrenaline into the heart.

This is the first fatal case following penicillin recorded by this hospital. Two years ago a severe case of shock was observed following the injection of 400,000 units of procaine penicillin given to a syphilitic patient.—I am, etc.,

E. H. R. ALTOUNYAN.

Aleppo, Syria.

The College of General Practitioners

SIR,—I rather gather that the movement for higher criteria for future membership of the College of General Practitioners is stronger at the moment in Scotland than it is in England. It is to be hoped that the desire for this will gain momentum in all quarters. It has been clear to me since the College was mooted in the early days of the Steering Committee that, if it is to secure equality for general practitioners with other sections of the profession, it must become, first, a royal incorporation, and, secondly, a licensing body able to issue a diploma or diplomas which will be recognized by the General Medical Council as a registrable higher medical qualification or qualifications.

Whether foundation or early members will automatically receive this diploma or not is of lesser importance at the moment. Nor is the form that the examination for the diploma should take at present in question. I do not wish to complicate the issues by referring to these disputable matters, but I do feel that at the moment the College enjoys widespread good will. To delay unduly in applying for a royal charter and in establishing a registrable diploma would, in my judgment, be most unfortunate.—I am, etc.,

Glasgow, W.3. J. INGLIS CAMERON.

Research in General Practice

SIR,—The annotation entitled "Research in General Practice" (*Journal*, November 28, p. 1209) mentions herpes zoster as a suitable subject for study. It may be of interest to report that a small group of general practitioners working in rural areas of central Perthshire has been recording its observations on this disease for the past two and a half years. Our records are made on a standard form drawn up by Dr. P. L. McKinlay, the medical statistician to the Department of Health for Scotland.

As the majority of the members of our group are now foundation members of the College of General Practitioners it is our intention at an early date to explore the possibility of making our local inquiry the nucleus of a much bigger investigation conducted under the auspices of the College.—I am, etc.,

Pitlochry JOHN M. HENDERSON.

Alcohol-induced Pain in Hodgkin's Disease

SIR,—Pain induced by alcohol is not peculiar to Hodgkin's disease. During the Libyan campaign of 1941 I suffered from a Brodie's abscess in the head of the right tibia. One half-glassful of beer was sufficient to cause pain of distressing severity in the region of the lesion. After confirming this curious phenomenon on two or three occasions with several types of alcohol-containing drinks, I was forced temporarily to become teetotal.

Before operative cure of the abscess I discussed the possible cause of such pain with Lieutenant-Colonel Graham, O.C. Surgical Division, 2/1 Australian General Hospital. He had himself suffered from a pyogenic infection of bone, and had experienced a similar alcohol-induced pain. We thought that the probable explanation was traction upon pain-sensitive structures (? vessels) caused by vasodilatation in osteoporotic tissue.

Growth of Hodgkin's tissue in bone may have been the cause of the pain in all instances quoted by Dr. Jan G. de Winter (*Journal*, September 12, p. 604). I have not known such pain to occur after alcohol in several other cases of pyogenic osteomyelitis, nor in cases of tuberculous osteitis and myelomatosis.—I am, etc.,

Victoria, Australia. D. A. ALEXANDER.

Agonal Myokymia

SIR,—Recently I watched an old lady die of hypertensive heart failure. About half a minute after I heard the last heart sound the entire chest wall and shoulders rippled with fibrillary contractions of the muscle fibres. This went on for about a minute. The face was not affected and the rest of the body was covered. The room was warm and there was no perceptible draught. It was a most striking sight.

I have never heard of this phenomenon and can recall no reference to it in the literature. One seldom sees the act of dying; one feels that were myokymia frequent at this time the ancients would have been well aware of it and that it would be described in classical writings. The only explanation I can suggest is that I saw during a minute an effect of anterior horn-cell degeneration which takes place over months in motor neurone disease.—I am, etc.,

Hutton Mount, Essex. GAVIN THURSTON.

Medresco Hearing-aids

SIR,—Your leading article of October 24 (p. 929) dealing with Medresco hearing-aids states: "There is no doubt that the benefit extended to so many deaf people by the Medresco aid is ample return for the trouble and cost of providing a hearing-aid service on a national scale." The Medresco service has now been operating for nearly five years, and it would be wise to ask whether or not we are getting the best value for the money expended, this value to be determined in terms of hearing rehabilitation or the extent to which the hearing-aids distributed have enabled those who have received them to lead a normal life, free from the handicap of deafness. Judged in this way, the Medresco service may be found to have several serious shortcomings:

Mr. Gray and Miss Cartwright in a survey carried out for the Ministry of Health and summarized in the *Lancet*[1] reported that the average daily use of the Medresco was 4.9 hours, and that only 18% of the aids issued were ever taken to work. The personnel of clinics have been consistent in their advice that only about one-third of the aids issued received any real use, one-third received occasional use, and the remainder were not used at all. The exclusion of commercial hearing-aids from the Health Service means that the hard-of-hearing are denied new developments as they become available. Bone conduction has just been introduced after being fully developed more than 20 years ago. Automatic volume compression, which has been featured in commercial hearing-aids for the last five years, has not yet been introduced, although it is essential in many types of inner ear deafness.

Might we not as a nation get better value for the money expended if some of this were devoted not to the giving away of free hearing-aids but to a determined drive to detect and treat deafness immediately it occurs, and particularly in school-children?—I am, etc.,

A. EDWIN STEVENS,

London, W.C.2. President, Hearing-aid Manufacturers Association.

REFERENCE

[1] *Lancet*, 1951, 1, 1170.

Antibiotics in Bacteriaemia

SIR,—I was interested to read the account of a fatal case of staphylococcal bacteriaemia described by Drs. W. H. Jopling and F. D. Schofield (*Journal*, November 21, p. 1140). There are, however, two points which do not seem to have been considered by the authors. First, it is known that *in vitro* tests do not necessarily correspond to *in vivo* results. Thus it is perfectly possible for a patient to be cured of a bacterial infection by an antibiotic while *in vitro* tests demonstrate the organism to be insensitive to that antibiotic. Secondly, it is also known that bacteriaemias respond more satisfactorily to bactericidal drugs such as penicillin and streptomycin rather than bacteriostatic ones such as aureomycin and chloramphenicol. Such a bactericidal action is probably particularly important when the cellulo-humoral response, as in this case, was apparently defective.

For these reasons it is difficult to understand why the authors should have persisted first with repeated courses of aureomycin and secondly with 57 days of chloramphenicol in spite of repeated positive blood cultures. Apparently it did not occur to them, in spite of the results of the *in vitro* tests, that it would have been worth trying the effects of a drug such as streptomycin. Furthermore, it might also have been of avail to have given the latter drug in combination with massive doses of penicillin and benemid.—I am, etc.,

Waltham St. Lawrence, Berks. M. ANTHONY PEYMAN.

Succinylcholine Chloride for Casualty Anaesthesia

SIR,—Referring to the use of succinylcholine chloride ("scoline") in casualty practice, my personal technique varies from that of Drs. Terence Vaz and J. M. Bishop (*Journal*, October 17, p. 885). Instead of using gas for induction and then giving succinylcholine chloride, I use the bare minimum of thiopentone and give succinylcholine chloride as much as is needed judging by the age and weight of the patient. By this method I have done over 200 cases of casualty anaesthetics for minor operations. There has not been any ill-effect in this technique. Recovery has been quick, and the patients have looked very fit. Vomiting has not occurred in one single case. Those who have criticized Drs. Vaz and Bishop have not given the matter a thorough trial. If it was dangerous there would have been at least 1 case in 200 which would have shown some ill-effects.

The details of these 200 cases will, I hope, be published soon.—I am, etc.,

Sheffield. RASHBEHARI GHOSE.

Insulin Zinc Suspensions

SIR,—In view of the correspondence regarding the new insulin zinc suspension preparations, the following observations may be of interest. After the investigation into the use of these insulins on 28 patients which were reported by Dr. R. B. Wilson and myself (*Journal*, November 7, p. 1023), a further 42 patients were tried on these insulins in the Victoria Infirmary, Glasgow, prior to their general release on November 16. The majority of cases were similar to those in the original series, many requiring large doses of insulin (from 80 to 140 units in nine cases), but also included were nine new patients who had not previously received insulin. In this supplementary series satisfactory control was obtained with "lente" in 32, with "ultralente" in 2, with a mixture of lente and ultralente in 3, and with lente and "semilente" in 2, while in 3 cases change to the new insulin resulted in much poorer control.

In the combined series, comprising 70 patients, control was effected with a single daily injection of lente in 47 (67%), of ultralente in five (7%), and of mixtures of lente with ultralente or semilente in 10 (14%)—a total of 63 (88.5%). We have found, therefore, that lente is suitable for a majority of patients, but that the proportions of crystalline and amorphous insulins must be altered in an appreciable number of cases. In this regard, however, individual variations appear to be very great. Whereas lente insulin contains 30% amorphous, we found that the proportion of this in the mixtures required to control 10 of our patients were: 12%, 15%, 15%, 16%, 19%, 37%, 47%, 53%, 57%. I would agree with Drs. A. Stuart Mason and D. Verel (*Journal*, November 28, p. 1215) that it would be at least very premature to advocate an alteration in the proportions present in lente. Nevertheless, as very different proportions are required by some patients, the fact that ultralente is not available in the strength 80 units per ml. is a real disadvantage, as Drs. J. D. N. Nabarro and J. M. Stowers (*Journal*, November 7, p. 1027) have already pointed out.

It will be noticed that five of our cases were regarded as failures and it was interesting to find that Drs. A. Stuart Mason and D. Verel had had similar experience. One of these failures has been studied further. She had formerly taken 44 units of protamine zinc insulin, but immediately developed acute symptoms when given 44 units lente. Later it was found she obtained very good control, in fact considerably better than that with the previous protamine zinc, with a dose of 72 units lente. This produced slight hypoglycaemic symptoms in the forenoon and she is now being tried on a mixture with less amorphous insulin.

It seems that there are difficulties in changing some patients on to the newer preparations, and these difficulties require further investigation. It is to be hoped that a solution will be found, since eventually it seems very desirable that, as Dr. W. Oakley has said (*Journal*, November 7, p. 1021), both protamine zinc and globin insulins should be withdrawn. Admittedly no one would wish to change the regime of a diabetic under perfect control and so these older insulins may have to be continued for a considerable time, but I would suggest that they be abandoned forthwith for all new cases.

In our original paper we recorded no local insulin reactions with the new insulins. That such can occur, however, is apparent from the observations of Drs. Stuart Mason and D. Verel. Recently I have encountered two patients who have shown quite troublesome local reactions; both were new patients who had just started to take insulin, and it is not yet known whether this sensitivity will be overcome. Finally, it may be of some interest to record that in two of our patients using lente insulin marked fat atrophy was observed at the site of injection.—I am, etc.,

Glasgow. IAN MURRAY.

Medical Needs in the Gold Coast

SIR,—Having only recently returned from the Gold Coast after two tours of service, I was particularly interested in Mr. Ian Fraser's view (*Journal*, October 31, p. 987) on the shortage of medical officers there. I congratulate him on his keen appreciation of the causes of the present situation, following only a short visit to the colony. From the last paragraph of Dr. K. A. Taylor's letter (*Journal*, November 28, p. 1217) I can only assume that he has not had recent experience of the Gold Coast, and I hasten to assure him that conditions have drastically changed within recent years.

I think that the most important thing necessary to bring about an improvement is a change of heart and attitude in the non-medical administrators, not only in the Colonial Office, but also in the Gold Coast Government (which is now largely African). The present situation is that a European doctor is very unlikely to be offered a pensionable appointment, though he may easily obtain one under contract. From the specialist's point of view this is very important. To take up a post in the colonies is to cut your bridges behind you, for after spending several years outside the United Kingdom it is virtually impossible to be re-employed as a specialist on your return. Drs. G. L. Alexander and H. G. Calwell both make this point (*Journal*, November 28, pp. 1216 and 1217). If the Gold Coast wants specialists it must offer permanent posts. As Mr. Fraser states, "The expatriate specialist is more valuable to the colony the longer he stays."

Arising from this is the present rigid adherence to the "staff list," which lays down that there should be so many surgeons, so many physicians, etc. This adherence is quite absurd. One African surgeon who had his F.R.C.S., and who had been doing specialist work, was kept waiting for three years before being promoted from medical officer to a vacant specialist post. The administrators should realize that it is easier to alter staff lists than to obtain specialists.

Whatever our views are on self-government, it is undeniable that the new administration in the Gold Coast has greatly increased the burden of the ordinary medical officer. This is not made easy to bear by the application of discrimination against expatriates when it comes to study leave. It is now almost impossible for an expatriate to obtain much leave. This causes frustration to the individual and an overall loss of officers to the Service. This should be borne in mind by those who appear to find Africanization more important than their country's needs.

The Gold Coast remains a great challenge to our profession. Disease, curable disease, is there in plenty, and yet there is only one doctor to more than 50,000 inhabitants. But before going to work there we must be assured of our position, and that we will not be asked to practise alongside unqualified persons. Perhaps the B.M.A. can help, but in view of the glib but efficient way they were dealt with by the Colonial Office in the discussion on pay for medical officers in the Colonial Service, only a few years ago, they will have to improve their bargaining power. However, I feel that in Mr. Ian Fraser they have a powerful weapon, equipped as he is with first-hand knowledge and his grasp of the long-overdue improvements.—I am, etc.,

Edinburgh. D. B. SCOTT.

Press Publicity

SIR,—Many must deplore the sickening vulgarity which so often invests newspaper accounts of medical matters, such as remarkable operations. To members of the medical profession there are other grounds for concern; I mean the way in which the principal figures in such exploits are made to endure an improper publicity, and even to appear, by implication, to have given a "story" to the press.

Journalists, of course, have their living to earn, and know what the public wants; but the newspapers of this country still have a reputation for fundamental decency. If it could be made plain that a doctor's career might be in jeopardy were the Disciplinary Committee to take notice of these seeming improprieties, surely such objectionable practices would cease.—I am, etc.,

Birmingham, 15. B. M. WILLMOTT DOBBIE.

More Social Medicine

SIR,—I must beg the courtesy of your columns to clear up a misunderstanding on the part of Dr. C. Metcalfe Brown in the criticism he makes (*Journal*, December 5, p. 1254) of my statement in the book *Social Medicine*, on orthodox treatment of diabetes and asthma.

Dr. Metcalfe Brown ascribes to me the very view (the mechanistic approach to medicine) that I am criticizing. In fact, only a few lines later I write: "All these explanations and cures aim at the parts of the body which are mainly affected; none is aimed at the fundamental causes of the disorder as a whole; and we therefore cannot rely on an infallible cure from these methods."

On diphtheria immunization, the point I make is that its introduction on any effective scale in this country was not made until 1941. This, in fact, is the year in which it was introduced by the Ministry of Health, and is quoted in all their official publications. Indeed, it was not until after this date that any appreciable reduction in diphtheria was made in this country.—I am, etc.,

London, N.W.6. S. LEFF.

What is Enpepilo?

SIR,—In a Report to the General Board of Health on a preliminary inquiry into the sewerage, drainage, and supply of water and the sanitary condition of the inhabitants of the township of Middleton in Lancashire, the following statement occurs at page 18: "Other diseases have also been very prevalent, and assumed a malignant form, such as scarlatina, rubula, and enpepilo."

The report is by Robert Rawlinson, Esq., C.E., Superintending Inspector, and was printed in 1854 for H.M.S.O.

Can any of your readers suggest what disease may have been referred to by the term "enpepilo"?—I am, etc.,

Purley, Surrey. J. CAUCHI.

The Pain of Perurethral Manipulations

SIR,—As the *British Medical Journal* does not reach here until six to seven weeks after publication, my comments on Dr. E. C. Atkinson's letter (*Journal*, August 22, p. 440) are somewhat belated. If perurethral manipulations are carried out with gentleness and skill, an efficient topical anaesthetic can render them in most cases almost painless. The anaesthetic agent, however, must be efficient. It is surprising that some people still use, and that some writers of quite recent textbooks still recommend, procaine for this purpose. Procaine is not a surface anaesthetic.

I agree with Mr. H. P. Winsbury-White (*Journal*, September 19, p. 674) that the cocaine-sodium bicarbonate-chlorbutol combination, used as he advises, is most effective. I also have used it for years. It should be realized, however, that no matter how effective the topical anaesthetic agent, passage of instruments along the urethra will generally cause pain if the bladder neck is put on the stretch, or if the calibre of the instrument used is more than about 20 Fr. Like Dr. Atkinson, I have often wondered why some urologists make things so difficult for their patients and themselves by not using adequate anaesthesia.

Finally, Sir, may I make a plea for the use of the word "perurethral," which I have used throughout this letter? You will agree with me, I am sure, that no analgesic agent could mitigate the agony of the "transurethral" passage of an instrument.—I am, etc.,

Sydney, Australia. D. C. TRAINOR.

Lead in Lollies and in Water

SIR,—In commenting further on this question your correspondent, Dr. L. R. L. Edwards (*Journal*, November 21, p. 1160) asks: "Is this distinction of a decimal place dependent in the lollies controversy on whether we regard the ice lolly as a solid or a liquid?" The answer to this is that to an appreciable extent it is, because there is strong evidence that lead is absorbed by the body more readily from simple liquids than from foodstuffs generally, in which it is more likely to be in organic combination. Possibly this outlook may have been a reason for the comparison with drinking water in your annotation (*Journal*, September 12, p. 613). Some ice lollies have a substantial content of solid constituents, but a large proportion of them are mainly water; whatever their solids content, they melt, and it therefore seems reasonable to regard them as liquid supplied in a frozen condition. Lead in significant quantity is not a natural constituent of foodstuffs. A futher point which seems important is that ice lollies are consumed almost exclusively by young children, which is another reason for supporting the attitude in your annotation that the amount of lead allowed should be very low.

For drinking water an especially low limit is required because of the comparatively large volumes consumed. However, in mentioning "generally accepted maximum permitted quantity of lead in drinking water as 0.02 p.p.m." Dr. Edwards misunderstands my mention of this figure (*Journal*, October 31, p. 993), which was not given as a limit. As a maximum permitted quantity in water I mentioned the United States standard of 0.1 p.p.m.; the same figure would be widely accepted in this country.—I am, etc.,

London, S.W.1. ROY C. HOATHER.

The Human Foot

SIR,—It was interesting to read that 14.4% of the recruits in the survey reported by Mr. D. Hewitt and Drs. A. M. Stewart and J. W. Webb (*Journal*, October 3, p. 745) suffered from foot defects prior to enlistment, and it seems worth recording the amount of trouble to which foot defects gave rise in a recent survey of a planned cross-section of the Army. The survey was carried out by the Army Operational Research Group and recorded the number of men who reported sick with foot trouble during a period of four weeks. The results at present available show that 2.1% per week of 1,246 recruits reported sick with foot trouble (the figure compares with 1.8% per week which I reported from a smaller survey of 623 infantry recruits over a period of six weeks).[1] Of 3,578 trained men studied in north-west Europe 0.9% per week reported sick with foot trouble. If one considers only those who reported sick with foot defects similar to those considered by Mr. Hewitt and Drs. Stewart and Webb, the figure for recruits was 0.6% per week and for trained men 0.07% per week.

In order to reduce the incidence of foot defects, it appears that prophylaxis must begin in early life, as Dr. Doris Craigmile emphasizes (p. 749). Meanwhile there is much that can be done to prevent existing defects from getting worse and from causing symptoms. The Army lays particular emphasis on the following measures: (*a*) Careful fitting of all footwear: (*b*) education in the care of the feet and footwear; (*c*) personnel selection for various occupations (taking into account each man's medical category); and (*d*) the use of conditioning courses, where necessary, to develop the musculature and to correct postural defects.

I am grateful to the Director-General, Army Medical Services, to the Scientific Adviser to the Army Council, and to the Superintendent, A.O.R.G., for permission to publish this letter.—I am, etc.,

Bristol. GEORGE HUDSON.

REFERENCE

[1] *J. roy. Army. med. Cps.* In press.

Distinguishing a Psychopath

SIR,—I hesitate to add to the correspondence on the above subject (*Journal*, November 28 p. 1224), but Mr. Justice Hilbery says that he is collecting definitions of the term "psychopath" from various psychiatrists. I would like to add what is, I think, a commonsense one.

Mental diseases can be divided up into three large groups —mental deficiency, the neuroses, and the psychoses. A psychopath may not suffer from any of these and yet there is present a disease of the mind which tempts him to act in a certain manner on certain definite stimulation; which manner is clearly abnormal to his usual state and mental condition. Further, he frequently gives in to temptation, and neither risk nor punishment is a deterrent, and both are at times insufficiently potent to make him throw to one side his abnormal behaviour.

I shall now sit back and watch the legal and clinical pundits pull this to pieces, and pray that something good will come out of it.—I am, etc.,

Bromsgrove. ANDREW SHEPHERD.

Peritonitis and Antibiotics

SIR,—Mr. N. C. Lake (*Journal*, December 13, 1952, p. 1307) has mentioned the development of general peritonitis in patients being treated with antibiotics. Since 1948 I have seen in negroes, mostly women, 16 cases of general peritonitis with moderate or absent fever, slight general symptoms, and moderate distension of the bowels, proved by aspiration of pus through an ordinary syringe. These were treated by parenteral penicillin and streptomycin in large doses together with aspiration of the pus every day or every second day. All recovered, 14 without any operation whatever. One had a relapse one year later, the infection stemming from chronic salpingitis. The aetiology of the majority could not be ascertained. It may be said, however, that appendicitis is an unlikely cause, as it is extremely rare in the Central African negro, in whom symptoms of acute appendicitis, when they are found, more often have their origin in an inflammation of the iliac lymph nodes. In the local type of general peritonitis of low toxicity I feel that antibiotics are safer than an operation.—I am, etc.,

Stan, Belgian Congo. A. BARLOVATZ.

Florence Nightingale House

SIR,—Advanced work for nurses was an important aspect of Florence Nightingale's nursing policy. She wanted nurses of all nations to be what she called "missionaries of health" by training others and raising the standard of health wherever they went.

Next year will see the centenary of Florence Nightingale's mission to the Crimea. The National Florence Nightingale Memorial Committee in the United Kingdom is seeking funds to establish permanently a fitting memorial to her noble work and inspiration. It is proposed: (1) to endow a residence for 44 nurses of all nations while undergoing advanced courses in London; and (2) to further the advance of nursing education by the award of scholarships.

Throughout the world similar national committees are raising funds for the award of scholarships to nurses. They are all part of the Florence Nightingale International Foundation, which is concerned with nursing education internationally. The successful candidates come to Britain and reside at Florence Nightingale House at 173–175, Cromwell Road, London, S.W.5, during their postgraduate training, adding an additional responsibility to the committee in this country; but this is the land of Miss Nightingale's birth and we must not fail in our duty to her memory.

We therefore appeal to everyone who appreciates her magnificent work for the nursing profession, and to everyone who has experienced the kindness of a nurse, and to everyone who wishes to express in tangible form their gratitude. Please either send a donation or write for a copy of an informative and illustrated booklet to: The Florence Nightingale Memorial Committee of Great Britain and Northern Ireland, 12, Whitehall, London, S.W.1.—I am, etc.,

London, S.W.1. LUKE, Chairman.

POINTS FROM LETTERS

The Human Foot

Dr. R. C. GREENBERG (Harold Hill, Essex) writes: I would submit that it is very questionable whether a *pathological* condition of flat foot, *per se*, exists at all ("Any Questions?" November 14, p. 1114). It is very rare indeed that a truly flat foot is ever seen in childhood, and even then if one gets the child to stand on its toes the arch is clearly formed. Consideration of the treatment of the almost non-existent syndrome of flat foot in childhood can hardly be separated from the general problem of the treatment of conditions of the feet and legs, such as pigeon toes, knock knees, bow legs, valgus ankles, and so forth. It seems, from what information is available, that we doctors carry out a great many manœuvres for such conditions and most of them "get better"—which seems to mean the patients approach a socially acceptable norm of appearance and gait, but in fact they would get better just as soon without anything being done at all. It would seem reasonable to reserve treatment for the more gross abnormalities of form and those malfunctions which are definitely pathological and not just physiological variations of normal. The amount of time and money involved is, by the way, not inconsiderable. Luckily we can all agree on one thing: that whatever is done for a child's feet will be set at naught if those feet remain encased in unphysiological, ill-fitting shoes.

Dr. A. B. PARTRIDGE (Northampton) writes: In 1947 and 1948 I bought two pairs of war-surplus Army boots which I was told had been designed for African infantry who had never worn boots before. The soles are perfectly straight along the medial border, and a pair standing together is as broad as it is long. They are the only boots in which my toes really reach to the tip when walking steeply downhill, instead of my feet being pinched across the heads of the metatarsals. My usual tendency to ingrowing toenails ceases when wearing them. I have only one regret: that I did not buy a dozen pairs while they were available. Dr. G. G. Sherriff's comparison with the binding of women's feet in China (*Journal*, November 7, p. 1048) is a perfectly fair one. We must continue, perforce, to "bind" until manufacturers and the public realize that the straight inner border is the normal shape for the normal foot.

Cataract and Blindness

Dr. M. W. BIRD (Wells) writes: I am surprised that the observation in your annotation (*Journal*, November 7, p. 1038) on Professor Arnold Sorsby's report concerning the high incidence of cataract as a cause of blindness has not brought further comment in the *Journal*. Anyone who has anything to do with senile cataract patients knows that the reason for blindness is not mainly on account of inoperability due to age or illness but to the stubborn unwillingness of such patients to leave their home surroundings and undergo the ordeal of an operation in hospital. Surely, if these patients will not go to hospital, the ophthalmic surgeon should make an effort to go to them. I would suggest a well-planned system of domestic surgery. A team consisting of a surgeon and his assistant with a number of nurses should go out "on circuit.". . . I am sure that such a policy of domestic surgery would not be a retrograde step. With the aid of modern antibiotics, anaesthesia, and analgesia the results should be as good as, if not better than, the satisfactory percentages reported for surgery in rural India.

Insurance Against Misfortune

Mr. T. B. FITZ GERALD (Ashton-under-Lyne) writes: Would it not be a reasonable and possible arrangement for the Health Service, or individual hospitals, to insure patients against unavoidable risks, somewhat on the lines of "third party" insurance for road risks? The provision of reasonable financial help to such individuals and their families would soften the sting of misfortune, and should do much to lessen the urge to desperate or vindictive claims for damages.

Obituary

WILFRED SHAW, M.D., F.R.C.S., F.R.C.O.G.

We record with regret the death on December 9 at the age of 55 of Mr. Wilfred Shaw, surgeon in charge of the gynaecological and obstetrical department at St. Bartholomew's Hospital.

Born at Birmingham on December 12, 1897, the son of Isaac Shaw, J.P., Wilfred Shaw was educated at King Edward's School in that city and at St. John's College, Cambridge, which he entered with an open scholarship. He continued a brilliant student career at Cambridge by winning a foundation scholarship and exhibition and Wright's prize. In 1918 he obtained a first-class in Part 1 of the Natural Sciences Tripos, graduating B.A. in 1919. He then went on to St. Bartholomew's Hospital with a Shuter scholarship, and later won the Matthews Duncan gold medal, the Lawrence research scholarship and gold medal, and the Cattlin research fellowship. After qualifying in 1921 he held house appointments at Bart's and then continued his postgraduate studies in Vienna and Dublin. He was admitted F.R.C.S. in 1923, graduated M.B. in 1924, and proceeded to the M.D. in 1928, being awarded the Raymond Horton-Smith prize for his thesis. In 1930 he received a certificate of honourable mention for his dissertation submitted for the Jacksonian prize of the Royal College of Surgeons of England. Elected F.R.C.O.G. in 1932—he was a founder member—he served on the museum committee of the College from 1939 to 1949 and on the pathology committee from 1949 to 1952.

Shaw, who saw service as a surgeon-probationer in the Navy in the 1914–18 war, was so outstanding as a house-surgeon to Sir Charles Gordon-Watson that many of his colleagues thought he would make a career in surgery. He had a remarkably wide range of knowledge, and was a sound craftsman. But his chief interest lay elsewhere, and it is probable that Dr. Herbert Williamson, then physician-accoucheur to St. Bartholomew's, influenced Shaw's decision to take up the work of which he became so distinguished an exponent, his contribution to gynaecological pathology being especially noteworthy. After holding the appointment of chief assistant in the gynaecological department at St. Bartholomew's, Shaw was elected assistant physician accoucheur, and in 1946 became surgeon in charge of the gynaecological and obstetrical department of the hospital. He was also a member of the board of governors. Among other hospitals at which he held appointments were St. Andrew's Hospital, Dollis Hill, and Brentwood Hospital. When the B.M.A. held its Centenary Meeting in 1932 Shaw was one of the honorary secretaries of the Section of Obstetrics and Gynaecology, and five years later he acted as a vice-president of the same section at the Belfast meeting.

While still a comparatively young man Shaw was appointed examiner in midwifery for both Oxford and Cambridge, and later he acted in a similar capacity for the Central Midwives Board, the London Conjoint Board, the University of London, and the Royal College of Obstetricians and Gynaecologists. His rapid rise to fame as a gynaecological surgeon never obscured his interest in physiology and research, as his many outstanding contributions to the literature of his subject made very plain. He was the author of many papers—the last one published in this *Journal* being on the subject of the Martius operation for vesico-vaginal fistula—and several books. His *Textbook of Gynaecology* reached its sixth edition in 1952 and his *Textbook of Midwifery* has run to three editions.

Shaw's approach to his subject was essentially that of a scientist. He was quiet in manner and retiring in nature, yet he had an inexhaustible interest in his students and their subsequent careers, and a devotion to his own hospital that found an outlet in many ways that were deeply appreciated by those who knew him well. The tragic death of his old chief, Dr. H. Williamson, came as a great shock to him at the time, and in a sense left him with a feeling of isolation. Those who belonged to the Decennial Club of Bart's which included his year will long remember his persistent but unobtrusive efforts as one of its secretaries to keep it alive and active.

He is survived by his widow, three sons, and a daughter.

We are indebted to Dr. MALCOLM DONALDSON for the following appreciation: The death at an early age of my friend and colleague, Wilfred Shaw, is not only a great loss to all his friends but deprives gynaecology of one of its most scientifically minded members. "Wilfred," who was nearly always spoken of by his Christian name, was never more happy than when he was working in his laboratory, where he did his classical work on the histology of the ovary. This is not the time to recite a list of all the scholarships and gold medals that he was awarded, but mention must be made of his two textbooks, which are so popular that many editions have been published: he was just completing yet another edition at the time of his death. He will be mourned by his colleagues, many friends, and patients, and our heartfelt sympathy goes out to his widow and children.

J. H. writes: The untimely death of Wilfred Shaw has deprived British gynaecology of one of its best brains. Scientist, investigator, anatomist, pathologist, surgeon, and author are titles to which only one or two men in his specialty can lay claim: his versatile genius achieved them all.

Others will have chronicled the long and brilliant list of his academic awards. His best-selling *Textbook of Gynaecology* and his many famous publications in this and other journals made his name a household word not only to every student but to a wide international public. His operative sessions at Bart's were thronged with a polyglot and many-coloured audience, and here he delighted to demonstrate his latest modifications of some operation for prolapse or stress incontinence. On these occasions he invited and enjoyed criticism, and always maintained that he learned as much from his juniors as he taught them.

Essentially a shy, modest, and sensitive person, he was at his most natural when alone with one or two friends, with whom he would discuss a bewildering and fascinating range of subjects. He had a great sense of humour and never tired of pulling his own leg, as well as those of his beloved students, though nothing pleased him more than a deft repartee from his victim. His memory was remarkable, and he never forgot the name of any of the vast

number of students who passed through his hands. This uncanny gift enabled him to imprint indelibly upon his mind the published work of his specialty, so that his erudition and accuracy startled and confounded his opponent.

He knew and loved every stone and shadow in the Square at Bart's; here of a summer's afternoon he delighted to stand by the fountain and receive the greetings of all who passed that way. As we approached, his face would light up with a welcoming grimace and we would tarry a while in conversation. Having a word with Wilfred often implied more than pleasant chatter, and a few minutes of his shrewd advice and sound wisdom have resolved many a problem and helped many a career.

That a spirit so young and gay should be mortally wounded for the last two years did not daunt his matchless courage. Knowing his days numbered by a disease whose advance he observed almost weekly, he set himself the task of writing one last book. It was a race against time, but he was always a quick operator, and he has fulfilled his contract.

T. Y. FINLAY, M.D., F.R.C.P.Ed.

Dr. T. Y. Finlay, former maternity and child welfare medical officer in Edinburgh, died there on November 28 at the age of 71. Of Scottish parentage, Thomas Yule Finlay was born in Paris, where he spent his early years. When the family returned to Edinburgh he attended the Royal High School and then proceeded to the University, where he graduated M.B., Ch.B. in 1907, taking the M.D. in 1912 with a thesis on haemophilia, for which he received high commendation. He was elected F.R.C.P.Ed. in 1927.

After graduation Finlay held resident posts at many of the hospitals in the city, where he came under the influence of such stalwarts as John Wyllie, J. W. Ballantyne, John Thomson, and Claude Ker, of whom he often spoke, and always with affection and gratitude. From 1913 till 1919 he was principal medical officer and medical superintendent of the Craiglockhart Poorhouse and Hospital, Edinburgh, where he carried out much valuable and original work among the children resident there. In 1915 he became associated with the Edinburgh Infant Health Centres Committee and acted as one of that organization's medical officers for infant welfare work.

Finlay was the unanimous choice of Edinburgh Corporation for the post of medical officer in charge of the maternity and child welfare section of the public health department when that section was brought into being in 1919. Under his wise guidance and direction and his happy knack of knitting voluntary and official activities into a co-ordinated whole, the section steadily extended its field, and the results achieved were remarkable. When he retired in 1947 well-deserved tributes were paid to his outstanding services on behalf of the mothers and young children of the city.

In 1919 he was appointed a member of the Scottish Committee on Child Life of the Medical Research Council and carried out nutritional studies on infants and young children for that body. In 1922 he was elected an assistant physician to the Edinburgh Royal Hospital for Sick Children, a post he held until 1932, when he was appointed senior assistant physician to the local municipal hospitals' children's unit. From 1939 till 1947 he was also honorary associate paediatrician at the Simpson Memorial Maternity Hospital. He was lecturer and examiner on diseases of children and child welfare at the university and at many other teaching organizations in the city. Though he may not have published a great deal, his papers were always carefully prepared and were accurate and well expressed.

Recognition of his sterling work on the care of children came when he was elected a member of the Association Internationale de Pédiatrie Préventive in 1933, and an honorary member of the British Paediatric Association, of which he was an original member, in 1947, and of the Scottish Paediatric Society. Throughout his whole medical career in Edinburgh he was closely associated with many local voluntary organizations concerned with the care of mothers and children, and after his retirement he flung himself whole-heartedly into the work of many of these. He was one of the founders, in 1923, of a voluntary committee to promote adoption of children, and this committee had its headquarters in a room in his department. Later it became known as the Scottish Association for the Adoption of Children, and he was its honorary medical officer and, for a few years after he retired, its treasurer. He was a member of the committee appointed this year by the B.M.A. to consider the present law in relation to adoption, and his wide experience was of great value during its deliberations.

The pioneering spirit of Dr. Finlay was doubtless kindled by his brother-in-law, Gaston Variot, of Paris, one of the leaders in France of the infant welfare movement, but it was certainly set aflame by Ballantyne and Thomson, to whom he always acknowledged his deep indebtedness. He spent his whole life among children, whom he loved and to whom he gave of his best. His approach to the child, well or sick, was gentle and sympathetic, his examination thorough. Diagnosis was based essentially on the clinical findings, supplemented where necessary by laboratory and other aids. With difficulties in infant feeding he was at his best, and his management and supervision of marasmic infants were models of care and patience.

Simple in his faith, he was a keen and active member of the Church of Scotland. A staunch upholder of family life, he was supremely happy in his own family circle, and the sympathy of his colleagues and friends goes out to his widow, daughter, two sons, and grandchildren.

By the death of Dr. CHARLES HOPE WADDELL at Coseley on October 21 at the age of 74 the Black Country of South Staffordshire loses one of its outstanding practitioners. Although born in California, he spent his boyhood in Northern Ireland, and qualified in 1906 from Queen's College, Belfast, with the Irish triple licentiate. After holding a resident appointment at the Royal Victoria Hospital, Belfast, he came to England and learnt the disciplines of general practice as an assistant at Hednesford, Staffordshire. Forty years ago he entered his real life's work when he took over the practice at Coseley, an industrial village in the heart of the Black Country, and there he continued till he handed over the reins to a younger colleague two years ago—apart from a period of service with the R.A.M.C. in the war of 1914–18. A man of outstanding personality, Dr. Waddell exemplified the immense influence for good that can be wielded by a practitioner long resident in, and devoted to, his locality. Not only did he serve his patients to the utmost of his ability and with untiring energy, but he also controlled them, and his affectionate nickname of "the King of Coseley" reflected this paternal relationship, which indeed is one of the hallmarks of a good doctor. Apart from his professional work, he played a leading part in the public life of the district, serving as medical officer of Coseley for a time

and later as a councillor, and in the days of the voluntary hospitals he was the mainspring of many local activities devoted to their support. A loyal member of the British Medical Association, there was no more regular attendant at meetings, and he was chairman of the South Staffordshire Division in 1926–7, as well as being for many years a member of the local insurance committee. Dr. Waddell was a man of great though sometimes rugged integrity, whole-hearted and untiring in all he did, occupying a niche of his own in our affections, so that his death leaves those of us who knew him well with a sense of permanent loss. At the funeral service the parish church of Coseley was packed by colleagues and friends from hospital and practice and local authorities, and by his old patients, all of whom were there to pay respect to the passing of a great personality.—J. H. S.

Dr. D. R. ALLISON, consulting physician to Withington Hospital, Manchester, died suddenly on November 9 at the age of 50. David Rhodes Allison, who was a Yorkshireman, was born on November 25, 1902, and was educated at Leeds University, where he graduated M.B., Ch.B., with honours, in 1925. In the same year he obtained the London conjoint diploma, and in 1926 proceeded to the M.D. After holding the post of house-physician at the General Infirmary at Leeds he went into general practice at Filey, in Yorkshire. In 1939 he obtained the M.R.C.P. with the object of becoming a consulting physician, and shortly afterwards he left Filey on being appointed chief clinical assistant at Manchester Royal Infirmary. Early in 1942 he entered the R.A.M.C. as a lieutenant and saw service in West Africa and India. He relinquished his commission in 1945 because of ill-health, having attained the rank of lieutenant-colonel. On return to civilian life he became for a time honorary physician to the Manchester Northern Hospital and visiting physician to Oldham Royal Infirmary, and was then elected consultant physician to Stockport and Withington Hospitals, and, more recently, to Stepping Hill Hospital, Stockport. Because of his ability, integrity, and warm personality he soon built up an extensive consulting practice. He was especially interested in cardiology and in the psychiatric aspects of medical conditions, and was the co-author with the late Dr. R. G. Gordon of a book entitled *The Uses and Limitations of Psychotherapy*. In 1950 his paper on pain in the chest wall simulating heart disease was printed in this *Journal*. His fatal illness was sudden and quite unexpected, for right up to the day of his death he was apparently in good health and the full vigour of life. He will be remembered by his friends as a kind and loyal colleague who would take infinite pains to help, and by his many patients as a good and kindly doctor of outstanding ability and integrity. He leaves a widow, a daughter, and a son, who is also a doctor.—E. H. K.

Dr. F. W. JOHNSON died at his home at Bawtry, near Doncaster, on November 17, at the age of 77. The son of the late Dr. W. J. Johnson, Frederick William Johnson was born at Tickhill, Yorkshire, on October 14, 1876, and was educated at King Edward VI School, Retford, and at the Yorkshire College, Leeds, then a constituent college of the Victoria University of Manchester, where he graduated M.B., Ch.B. in 1899. After working as house-surgeon to Mr. Berkeley (later Lord) Moynihan at the General Infirmary at Leeds he went to South Africa to serve as a civil surgeon in the South African war, but was invalided home in 1901 after an attack of enteric fever. He then joined his father in practice at Bawtry. Always an enthusiastic member of the volunteer movement, he had remained attached to the Sherwood Foresters after his return from South Africa, and on the outbreak of war in Europe in 1914 he went to France with the R.A.M.C. From 1917 to 1919 he commanded a field ambulance, and was demobilized with the rank of lieutenant-colonel. In the last war he joined the Home Guard as medical officer to the South Yorkshire sub-area, with the rank of lieutenant-colonel. An active member of the British Medical Association for some 40 years, Dr. Johnson was chairman of the Doncaster Division from 1929 to 1936, and he was a former president of the Doncaster Medical Society. It was very seldom that he allowed anything to interfere with his attendance at meetings. He had the cheerful ruddy complexion of the countryman, a figure which always conveyed the hint of a military training, and the shrewdness and sagacity of the very best type of general practitioner. Many of his colleagues had the privilege of serving under his chairmanship of the Ministry of Labour and National Service board at Doncaster from 1939 to 1952, and were always impressed by his rapid and accurate clinical assessments: few men can ever have made fewer mistakes. A devoted churchman, he was for many years a churchwarden at Bawtry. In his early days he enjoyed playing football and cricket, and throughout his life he was a keen naturalist and gardener. The B.M.A. has lost a staunch supporter, general practice a wise, unassuming, and sterling character, and his colleagues a loyal friend. He leaves a widow, one son, Dr. F. H. W. Johnson, who carries on the practice, and three daughters.—R. W. L. W.

Dr. CAROLINE WALKER, who died suddenly on November 26, was one of those who helped pioneer the way for women to be doctors, and one of the oldest medically qualified women in the West of England. She was the trusted friend of many. Theodosia Caroline Green was born in January, 1872, one of the eleven children of the Reverend John H. B. Green, rector of Normanton-le-Heath, Leicestershire. From school days she was always one who was prepared to plough a new, and at times an unconventional, furrow. At school she studied geology on her own, as there was no one to teach it. When she decided to study medicine she again found difficulties in her way, and had to study in various places, first in London at the London School of Medicine for Women (now the Royal Free Hospital) and later at the Rotunda Hospital, Dublin, where she obtained a licence in midwifery in 1895. Later in the same year she took the Scottish triple qualification, and then went on to Brussels, where she graduated M.D. in 1896. After qualification she took a post as junior assistant medical officer at the Lincolnshire County Asylum, an event which evoked a newspaper headline, "Woman Doctor Comes to Lincoln." In 1900 Caroline Green married Mr. Cyril H. Walker, then an ophthalmic surgeon practising in Bristol. For the next 30 years, especially during the first world war, she busied herself with infant welfare work, and acted as medical officer at several clinics in Bristol. For some years she lectured in hygiene in the department of education of Bristol University. She became well known, not so much for academic achievement or clinical skill as for her very sound advice, which was often sought and freely given on a wide range of subjects related to medicine. She was the much respected member of many committees, some medical and some connected with social welfare. Most of all, perhaps, her wise and balanced advice was valued during the 15 years that she was chairman of Walker Dunbar Hospital Committee. However, it was not only hospitals and welfare organizations which received her help: her friendly counsel was sought by many, particularly young women doctors, in whom to the end of her life she had a special interest. After an accident in 1938 she became a partial invalid, but in spite of increasing pain and disability from arthritis she remained resolutely cheerful, her courage and fortitude encouraging many in similar circumstances. Her generosity, sense of humour, and high Christian principles brightened every part of her life and work, whether for medicine or for her local church. We offer our deepest sympathy to her husband and to their two sons, one a doctor, and three daughters. One grandson is also a member of the medical profession.—D. H. T.

Professor HANS ISELIN, the eminent Swiss surgeon, died at Lörrach, Baden, on November 22, at the age of 75. He was born on February 21, 1878. His family were well known in Basle, and on his mother's side he was a descendant of Hans Holbein the younger. He studied medicine at Geneva and Kiel, graduating in 1902, and then joined the staff of the medical faculty at Basle University and later became chief of the surgical polyclinic in that city. He was

also surgeon to St. Clara-Spital and to St. Elisabeth Hospital, Lörrach, Baden. In 1918 he was given a professorial chair at Basle to develop the teaching of traumatic surgery, and he served for a time as dean of the medical school. Iselin was a pioneer in the use of radiotherapy in surgical tuberculosis and in the post-operative treatment of cancer of the breast. He made notable investigations on growth disturbances in rats after parathyroidectomy and published many papers on fractures and dislocations, bone and joint diseases, and traumatic surgery. He remained in active practice to the end of his life and was operating at the hospital in Lörrach on the day before he died.

Medico-Legal

CHOKED BY FAULTY MAGILL TUBE

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

At an inquiry held recently by the Sheriff-Substitute of Lanarkshire into the death of Miss Margaret Elliott, aged 32, in the Southern General Hospital, Glasgow, death was found to be due to a defect in the Magill tube used for the administration of a general anaesthetic which had never previously been known to the consultant anaesthetist, Dr. J. R. Gallie.

Miss Elliott was suffering from a recurrence of symptoms of cervical rib which had previously been much improved by operation, and was admitted to hospital for further operation to relieve pressure on the nerves running down from the neck to the left arm. Anaesthesia was induced by thiopentone, nitrous oxide, and oxygen, and 1.5 ml. "scoline" intravenously, and the assistant anaesthetist, after inflating the patient's lungs with oxygen, passed a cuffed Magill's endotracheal tube connected to a semi-closed anaesthetic apparatus. The tube was visually inspected on removal from the sterile drum in which it was stored, and the cuff on test inflation with the standard 10 ml. of air appeared to be in good condition. It had probably been used only once before. A throat pack was inserted round the tube to keep it in position, and anaesthesia was maintained with nitrous oxide, oxygen, and "trilene."

After some thirty minutes the anaesthetist noticed a sudden diminution in the volume of tidal air indicating obstruction of the airway. He deflated the cuff of the Magill tube, which caused the obstruction to disappear, and called the surgeon's attention to the obstruction. The operation was suspended, and cardiac massage restored the pulse, which had stopped. Voluntary respiration, which had also stopped, was re-established within a few minutes, but although the patient survived for eleven days her condition gradually deteriorated and consciousness never returned.

Section of the brain on necropsy showed mottled pink degenerative changes of the cortex and basal nuclei, and Dr. W. P. Weir, pathologist to the Royal Alexandra Infirmary, Paisley, concluded that death was due to anoxaemia of the brain following cessation of respiration and circulation during the general anaesthesia for the operation.

When the Magill tube was examined after the operation it was found that the rubber of the cuff was perished and that when the cuff was inflated the perished rubber blew up into a soft blister or bulb. Dr. Weir thought that this must have slid down the trachea and either pressed the open end of the tube against the side of the trachea and so blocked it, or else must itself have covered and blocked the end of the tube. A movement of the tube during the operation would have been sufficient to move the blister in this way. The tube had been kept after sterilization in the autoclave in the recognized way, and the only cause suggested for the deterioration in the rubber of the cuff was that a drop of ether or trilene, both of which are rubber solvents, might have got on it. This would explain why the defect was not shown by the test inflation of the cuff before the tube was used. Dr. Gallie in his evidence at the inquiry said that it was the first time that he had ever seen a rubber cuff fail in this way.

Medical Notes in Parliament

Fluoridation Experiments

Mr. IAIN MACLEOD, Minister of Health, informed Mr. C. R. HOBSON on December 10 that before fluoride was added to the water supplies of selected communities baseline information on the incidence of dental caries in those communities would be obtained and any comparable communities that could be used as controls. Other matters receiving consideration included whether a survey of fluoride excretion in the urine of representative children and adults of all age groups throughout the country should be made in order to assess the required dose of fluoride to be added to water supplies; how adequate supplies of fluorides in the most suitable form will be obtained; and what safeguards there will be against errors in dosage and undue exposure of the operating personnel to the materials handled.

Vaccination Deaths

Mr. S. P. VIANT asked the Minister of Health, in regard to the age group 0–5 for each of the years 1938 to the latest date available, how many death certificates were received on which the words vaccination, vaccinia, post-vaccinal encephalitis, or any other association with vaccination appeared, and how many of these deaths were assigned to vaccinia, generalized vaccinia following vaccination, post-vaccinal encephalitis, or other complications of smallpox vaccination. Mr. IAIN MACLEOD on December 8 gave him the following details:

Year	*Death Certificates with mention of Vaccinia, etc.*	*Deaths Assigned to Vaccinia, etc.*
1938	6	5
1939	1	1
1940	7	6
1941	4	4
1942	5	3
1943	4	4
1944	9	8
1945	6	5
1946	3	1
1947	10	6
1948	6	4
1949	1	1
1950	—	—
1951	6	4
1952	3*	3*

*Includes one infant who had not herself been vaccinated.

Health in British Guiana

Mr. RONALD RUSSELL asked the Secretary of State for the Colonies what improvement had been achieved in the health of the people of British Guiana in recent years. Mr. LYTTELTON stated on December 8 that, of the major communicable diseases in British Guiana, malaria had decreased substantially from 15,490 notified cases and 290 deaths in 1947 to 181 cases and 28 deaths in 1952. There had also been a decline in the number of notified cases of enteric fever and pulmonary tuberculosis. Other detailed improvements were too complex to summarize, but over the past eight years the infant mortality rate had fallen from 101 per thousand live births to 82, and over approximately the same period the expectation of life at birth had increased by four years.

Welfare Foods

Major G. LLOYD-GEORGE, Minister of Food, who was asked what he was doing to encourage the consumption of welfare foods, replied on December 7 that he welcomed the opportunity of assuring the House that by all the means at his disposal the Ministry continued to emphasize the importance of welfare foods. Mr. SOMERVILLE HASTINGS asked him to state in a few words how he was going to encourage an increased consumption of welfare foods. Major LLOYD-GEORGE said that many methods had been used for a considerable time—posters, talks, and full information to

expectant mothers. Every possible method was still being used, and the percentage of take-up of the various welfare foods remained much the same and had sometimes increased.

Student Nurses' Call-up

Mr. R. J. MELLISH asked the Minister of Labour on December 8 whether he proposed to exempt from national service all those employed as student nurses in mental hospitals, in view of the shortage of mental hospital staff. Mr. HAROLD WATKINSON, the Parliamentary Secretary, replied "No," but the call-up of such students could be deferred until they had completed their training.

Rejections

The numbers of men called up for national service, and the numbers rejected on medical grounds, in the past five years, it was stated by the Parliamentary Secretary, Ministry of Labour, on December 1, have been: 1948—150,900 (rejected, 27,750); 1949—166,600 (rejected, 36,370); 1950—174,200 (rejected, 47,314); 1951—168,651 (rejected, 43,856); 1952—170,384 (rejected, 42,829).

Hospital Service Reserve

Mr. IAIN MACLEOD, Minister of Health, announced on December 3 that the Queen had been graciously pleased to assume the title of Head of the National Hospital Service Reserve in the United Kingdom, thus extending to that Reserve the honour already conferred upon the Civil Defence Corps.

Universities and Colleges

UNIVERSITY OF OXFORD

The Theodore Williams Scholarship in Physiology has been awarded to Roger James Robinson, scholar of Balliol College, and Kenneth Bryson Roberts (Lincoln College) has been re-elected to the Philip Walker Studentship in Pathology for two years from October 1, 1953.

UNIVERSITY OF CAMBRIDGE

Dr. B. H. G. Hayward has been elected into a second John Lucas Walker Studentship for one year from June 1, 1952, and into the same studentship for two years from June 1, 1953.

In Congregation on October 17 the degrees of M.B., B.Chir. were conferred on G. G. K. Parsons.

UNIVERSITY OF ST. ANDREWS

At a Graduation Ceremonial held on October 9 the degree of M.D. (with commendation) was conferred upon J. A. Gillespie.

UNIVERSITY OF LONDON

The following candidates have been approved at the examinations indicated:

ACADEMIC POSTGRADUATE DIPLOMA IN CLINICAL PATHOLOGY.—P. B. Adamson, J. D. Arneaud, L. R. Chapman, S. K. Chopra, B. R. Davis, N. U. C. Godfrey, W. F. Hunter, S. Jatinandana, N. C. March, Mary Ralston, W. A. Russell, M. P. K. Shoobridge, J. C. Squires.

EXTERNAL DIPLOMA IN CLINICAL PATHOLOGY.—M. C. Berenbaum, M. Datta, H. J. Woodliff.

The following candidates at the London School of Hygiene and Tropical Medicine have been approved at the examinations indicated:

ACADEMIC POSTGRADUATE DIPLOMA IN PUBLIC HEALTH.—P. P. M. Browne, J. Clearkin, K. A. Rahman, J. T. Subramaniam, D. R. Thomson, D. Ungar.

ACADEMIC POSTGRADUATE DIPLOMA IN TROPICAL MEDICINE AND HYGIENE.—P. Sirivorasarn.

UNIVERSITY OF WALES

The Council of the Welsh National School of Medicine has appointed Cecil Wilfred Dickens Lewis, M.Ch., F.R.C.S., who is at present Lecturer in Surgery, to be Senior Lecturer in Surgery at the School.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **November 28** (No. 47) and corresponding week 1952.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1953					1952				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond	Scot	N. Ire.	Eire
Diphtheria	16	2	12	0	2	41	4	13	0	1
Dysentery	399	64	159	5	1	158	29	57	0	
Encephalitis, acute	1	0	1	0		3	0	0	1	
Enteric fever:										
Typhoid	2	0	0	0		3	0	0	2	1
Paratyphoid	3	0	0	0		8	1	0	0	
Food-poisoning	121	12		0		77	17		0	
Infective enteritis or diarrhoea under 2 years				25	17				6	18
Measles*	875	20	31	12	74	12,130	1129	174	24	178
Meningococcal infection	32	4	13	4	2	28	1	16	0	3
Ophthalmia neonatorum	26	3	7	0		35	2	10	0	
Pneumonia†	557	36	156	9	1	519	46	341	3	
Poliomyelitis, acute:										
Paralytic	50	4	13	3	7	62	3	6	1	2
Non-paralytic	27	3				21	2			
Puerperal fever§	211	48	20	3	1	227	36	11	3	1
Scarlet fever	1,484	75	286	48	59	2,226	188	370	38	83
Tuberculosis:										
Respiratory			157	20				134	31	
Non-respiratory			19	4				36	12	
Whooping-cough	2,608	114	366	50	49	1,854	108	97	36	96

DEATHS in Great Towns	1953					1952				
	Eng. & Wales	Lond.	Scot.	N. Ire	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0		0	0
Dysentery	0	0	1	0		0	0		0	
Encephalitis, acute		0			1		0			0
Enteric fever	0	0	0	0		0	0		0	
Infective enteritis or diarrhoea under 2 years	7	0	3	0	1	7	0	2	0	0
Influenza	6	1	1	0	0	11	1		0	1
Measles		0	0	0	0		0		0	0
Meningococcal infection		0	0				1			
Pneumonia	236	45	20	4	2	190	31		9	6
Poliomyelitis, acute	0	0			0	5	0			0
Scarlet fever		1	0	0	0		0		0	0
Tuberculosis:										
Respiratory	104	13	16	0	4	133	18	15	4	2
Non-respiratory		0	3	0	0		0	2	2	0
Whooping-cough	2	0	0	0	0	1	0		0	0
Deaths 0–1 year	194	25	23	2	11	206	18	33	10	11
Deaths (excluding stillbirths)	5,036	790	541	95	141	5,302	753	569	112	137
LIVE BIRTHS	6,802	1022	782	202	389	6,701	955	715	207	323
STILLBIRTHS	175	19	18			183	17	20		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

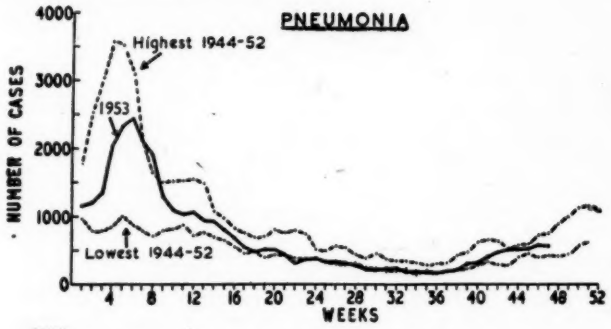
Vital Statistics

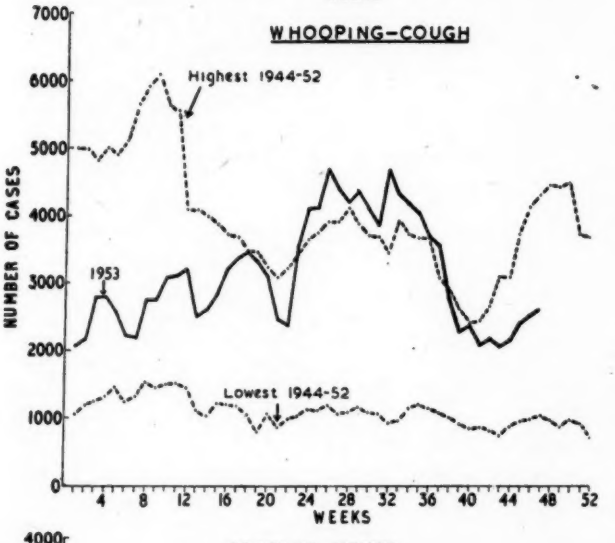
Northern Ireland—Second Quarter

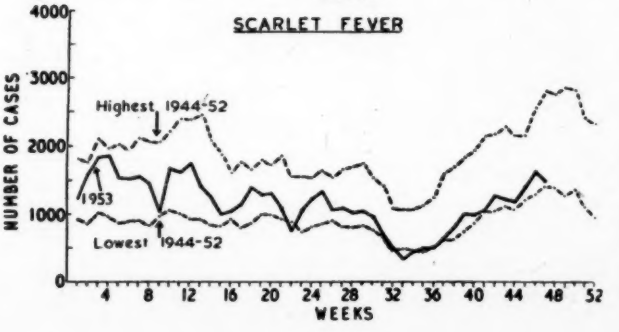
According to the Registrar-General's return of vital statistics for the quarter ending June 30 the birth rate was 22.9 per 1,000 population, an increase of 0.7 over the rate for the same period of 1952. The general death rate was at 10.8 per 1,000 of the population as compared with 10.7 for the corresponding period of 1952, but it is 0.4 below the average rate for the second quarters of the previous five years. The infant mortality rate of 37 per 1,000 live births was the lowest ever recorded for the June quarter, as was the death rate from tuberculosis (0.22 per 1,000 population).

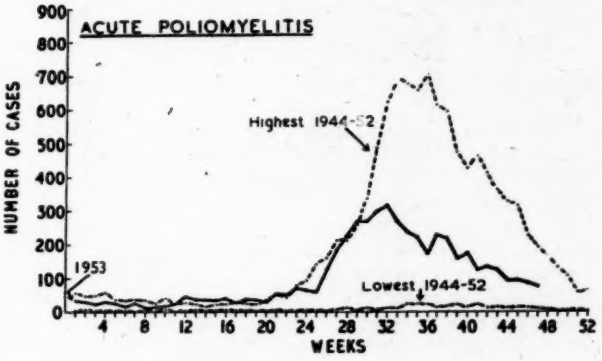
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1944–52 are shown thus - - - - - - -, the figures for 1953 thus ————. Except for the curves showing notifications in 1953, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

An increase of 98 in the number of notifications of whooping-cough, from 2,510 to 2,608, and 82 for measles, from 793 to 875, and a decrease of 129 for scarlet fever, from 1,613 to 1,484, were reported in England and Wales during the week ending November 28.

The largest variations in the trends of whooping-cough were a decrease of 49 in the number of notifications in Lancashire, from 276 to 227, and a rise of 33 in Essex, from 153 to 186. The largest rises in the incidence of measles were 59 in Norfolk, from 16 to 75, due to an outbreak of 65 cases in Norwich C.B., and 32 in Southampton County, from 6 to 38, due to an outbreak in Southampton C.B. with 21 notifications. The only large variation in the trends of scarlet fever was a fall of 32 in Middlesex, from 84 to 52. 16 cases of diphtheria were notified, 12 fewer than in the preceding week. The chief feature of the returns was a fall in Birmingham C.B. from 7 to 3. 5 cases were notified in Staffordshire. In Scotland 12 cases of diphtheria were notified; of these 9 were reported from Glasgow.

During the week 77 cases of acute poliomyelitis were notified. These were 4 fewer for paralytic and 7 fewer for non-paralytic cases than in the preceding week. The largest returns were Somersetshire 12 (Wincanton R.D. 7), Lancashire 8, London 7, Dorsetshire 6 (Poole M.B. 3, Wimborne and Cranborne R.D. 3), Staffordshire 5, Warwickshire 5, and Yorkshire West Riding 5.

399 cases of dysentery were notified, being 37 more than in the previous week. The largest centres of infection were Yorkshire West Riding 73 (Bradford C.B. 45), London 64 (Islington 12, Southwark 17), Lancashire 52 (Manchester C.B. 15, Bolton C.B. 14), Norfolk 42 (Norwich C.B. 42), Essex 35 (Braintree R.D. 14, Colchester M.B. 11), and Middlesex 34 (Willesden M.B. 34).

Week Ending December 5

The notifications of infectious diseases in England and Wales during the week included scarlet fever 1,549, whooping-cough 2,595, diphtheria 13, measles 886, dysentery 445, acute poliomyelitis 65, paratyphoid fever 1, and typhoid fever 3.

The Services

A *Supplement* to the *London Gazette* has announced the following awards:

Second Clasp to the Army Emergency Reserve Decoration.—Major W. H. Valentine, O.B.E., R.A.M.C.

First Clasp to the Army Emergency Reserve Decoration.—Major (Honorary Lieutenant-Colonel) A. W. Davidson, M.C., and Major R. L. Sadler (retired).

Army Emergency Reserve Decoration.—Major C. M. Fraser (retired).

The names of Captains E. D. Mackie and C. L. Tutty, R.A.M.C., appear in a list of those mentioned in dispatches in recognition of gallant and distinguished services in Korea during the period July 1 to 27, 1953.

Medical News

Nuffield College of Surgical Sciences.—At a meeting of the council of the Royal College of Surgeons on December 10 it was decided to proceed at once with the building of the Nuffield College of Surgical Sciences. It is almost exactly five years since the announcement of Lord Nuffield's magnificent gift of £250,000 for the purpose of building a residential college where young surgeons, particularly from overseas, could live while undertaking advanced study or research. The new college will adjoin the present premises of the Royal College of Surgeons, on its east side. A drawing of it was printed in our issue of July 2, 1949 (p. 27).

Dope-peddling in Britain.—The extent of the illicit traffic in narcotic drugs in Britain is much less than reports in the lay press might suggest. According to the United Kingdom's annual report to the United Nations on the subject, last year there was no evidence of any regular or organized traffic in Britain. Hemp and opium remained the drugs most frequently encountered by the police; of the 87 persons convicted of having hemp 67 were of African, Indian, or West Indian origin, while all except three of the 60 convictions relating to opium concerned Chinese, most of them in Liverpool. It is clear that regular "doping" by adolescents is not the problem here that it is in New York. The case of an 18-year-old plumber's mate, if the statements made in court were true, is said to be the "first recorded instance in the United Kingdom of an adolescent regularly smoking hemp." The report states that 297 addicts were receiving drugs from medical sources in 1952. In the non-professional classes women addicts outnumbered the men by nearly two to one, but among 75 addicts from the professional classes (72 doctors, 2 dentists, and one pharmacist) only three were women.

Buckston Browne Prize Essay.—The Council of the Harveian Society of London has selected "The Medical Problems of the Overweight Patient" as the subject for the Buckston Browne Prize essay. The prize, which consists of a medal and £100, is open to any member of the medical profession registered in the British Isles or Dominions and is limited to candidates under 45 years of age. Essays must be sent in by December 1, 1954. Further particulars may be obtained from the hon. secretaries, Harveian Society of London, 11, Chandos Street, Cavendish Square, London, W.1.

Scientific Exhibition, Glasgow, 1954.—Those proposing to exhibit at the B.M.A. Annual Meeting in 1954 should apply as soon as possible. In view of the joint meeting with the Canadian Medical Association in Toronto in 1955 there will be no other B.M.A. Scientific Exhibition in this country until 1956. Full details and application forms are obtainable from the Secretary, British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1.

102 Not Out.—At the Whittington Hospital, London, on December 5 an operation was performed to repair a fractured femur in an old lady of 102. The next day this remarkable patient was up for 20 minutes, and the latest news is that nine days after her operation she is up for three hours each day.

Dangerous Drugs Act, 1951.—By an Order under this Act, which came into force on December 14, the salts of N-allyl*nor*morphine and any preparation containing this substance have been brought within the provisions of Part III of the Act.

David Anderson-Berry Prize.—On December 4 the president of the Royal Society of Edinburgh, Professor James Kendall, F.R.S., announced the award of the David Anderson-Berry Prize to Dr. John Read, of the Dunedin Medical School, New Zealand, for his work on the relationship between oxygen tension and the effect of *x* rays on the tissues.

Council of the Royal Society.—In addition to the president, Dr. E. D. Adrian, the following members of the medical profession are among those who have been elected to the council of the Royal Society: Professor E. G. T. Liddell, Professor R. A. McCance, and Sir Edward Mellanby.

British Association of Otolaryngologists.—The following have been elected officers for 1953–4:—*president:* Mr. V. E. Negus; *immediate past president:* Mr. H. V. Forster; *vice-president:* Mr. I. Simson Hall; *honorary secretary:* Mr. Myles L. Formby; and *honorary treasurer:* Mr. W. A. Mill.

Medical Golfing Society.—At the annual general meeting Mr. George Armitage was elected president and Brigadier H. L. Glyn Hughes captain for the coming year.

London Medical Orchestra.—The Orchestra is now holding rehearsals on Thursdays at 7.45 p.m. at the George Eliot School, Marlborough Hill, London, N.W.8. More playing members are wanted, and should apply to the secretary, Dr. E. V. Slaughter, 6, Oxford Court, Queens Drive, London, W.3.

COMING EVENTS

A Seminar on Foot Health will be held by the Central Council for Health Education at St. John House, Collingham Gardens, London, S.W.5, from February 23 to 27, 1954. The programme will include a lecture on "Foot Function" by Mr. T. T. Stamm, films and discussions, and visits to London shoe factories.

The Ophthalmological Society.—The annual congress will be held at Durham University from April 22 to 24, 1954. The main subject for discussion will be "Inflammatory Vascular Diseases Affecting the Eyes." There will also be short symposia on "Cyclodiathermy," "Changes in the Incidence of the Eye Affections of Coal Miners in the Past 25 Years," and "Gonioscopy."

British Association of Physical Medicine.—The annual meeting will be held at King's College Hospital, London, S.E.5, on April 30 and May 1, 1954. Further information may be obtained from the honorary secretary, 45, Lincoln's Inn Fields, London, W.C.2.

Association of Surgeons of Great Britain and Ireland.—The annual meeting will be held in Leeds from May 13 to 15, 1954. The subjects to be discussed include: "Hiatus Hernia," "Ulcerative Colitis," "Exophthalmos," and "Duodenal Diverticula." Further information may be obtained from the honorary secretary of the association, 45, Lincoln's Inn Fields, London, W.C.2.

The South African Medical Congress will take place in Port Elizabeth from June 21 to 26, 1954. Part of the programme is expected to take the form of a symposium on rehabilitation. Those who would like to contribute papers at the Congress are asked to communicate as soon as possible with M. G. Woolf, Organizing Secretary, P.O. Box 1137, Port Elizabeth, South Africa.

International Association of Gerontology.—The third congress of the association will be held in London from July 19 to 23, 1954. Further information may be obtained from the organizing Secretary, Mrs. A. Humpage, B.M.A. House South, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Applications should be made first to the institution concerned.

Monday, December 21

ROYAL EYE HOSPITAL.—5 p.m., Dr. T. H. Whittington: Convergence, Heterophoria, and Factors Affecting Binocular Vision.

Tuesday, December 22

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Mr. A. K. Monro: Hypostatic Eczema and Ulceration.

APPOINTMENTS

ANDERSON, T., M.B., Ch.B., D.P.H., County Medical Officer of Health and Principal School Medical Officer, Oxfordshire.

BODMAN, R. I., M.B., Ch.B., D.A., Anaesthetist (Consultant Grade), St. Peter's, St. Paul's, and St. Philip's Hospitals, London.

BROWN, H. MORROW, M.D., M.R.C.P.Ed., Consultant Chest Physician, South Derbyshire Area.

DONALDSON, RAYMOND JOSEPH, M.B., B.Ch., D.P.H., Deputy Medical Officer of Health for the City of Stoke-on-Trent.

ESSEX-CATER, A. J., M.R.C.S., L.R.C.P., D.P.H., D.C.H., F.R.A.I., Deputy Medical Officer of Health, Swansea County Borough.

EVANS, W. G., M.B., B.Chir., D.P.H., Medical Officer of Health for Scarborough Borough, Scarborough Rural District, and Scalby Urban District; Assistant County Medical Officer, North Riding County Council; and Divisional School Medical Officer.

GIBSON, J. BAIRD, M.B., Ch.B., D.A., Consultant Anaesthetist, Alnwick and Wansbeck, Hospital Management Committee.

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—R. N. Twistington Higgins, M.B., B.Chir., Part-time Registrar to the Department of Psychological Medicine; S. M. Singh, M.B., B.S., House-surgeon to Orthopaedic and Plastic Departments; C. H. MacD. Walker, M.D., M.R.C.P.Ed., D.C.H., Senior Medical Registrar to Thoracic Unit; E. D. R. Campbell, B.M., B.Ch., Part-time Registrar to Department of Physical Medicine; Teresa M. Coyle, M.B., B.Ch., D.O., Part-time Senior Registrar to Ophthalmic Department; A. L. Jeanes, M.B., B.S., Registrar to Department of Clinical Pathology; E. P. G. Michell, M.B., B.Chir., M.R.C.P., D.C.H.; I. S. Wallman, M.B., B.S., M.R.A.C.P., and Joan Angus, M.B., Ch.B., M.R.C.P., House-physicians; A. F. Ferguson, M.B., Ch.B., F.R.C.S., and Anne M. Calder, M.B., Ch.B., F.R.C.S.Ed., House-surgeons; Mary F. Thomson, M.B., Ch.B., Assistant Resident Medical Officer, Tadworth.

LIVERPOOL REGIONAL HOSPITAL BOARD.—R. B. Taylor, M.R.C.S., L.R.C.P., D.P.M., Whole-time Consultant Psychiatrist to Rainhill Hospital; T. P. Smith, M.R.C.S., L.R.C.P., D.P.M., Assistant Psychiatrist to Ormskirk and Southport areas; F. G. Anderson, M.B., Ch.B., D.M.R.D., Assistant Radiologist to Aintree and Walton Hospitals; Lucy M. B. Nelson, M.B., B.S., M.R.C.P., Assistant Chest Physician.

MANCHESTER REGIONAL HOSPITAL BOARD.—Betty Hargreaves, M.B., Ch.B., M.R.C.O.G., Consultant Obstetrician and Gynaecologist, Wigan and Leigh Hospital Centre; J. D. Glynn, L.R.C.P.&S.I., D.P.M., Assistant Psychiatrist, Whittingham Hospital.

MASON, S. JOAN, M.B., B.Ch., D.O.M.S., Assistant Ophthalmic Surgeon for Newport and East Monmouthshire, North Monmouthshire and Rhymney and Sirhowy Valleys Hospital Management Committee.

MILNE, JOHN COUTTS, M.B., Ch.B., D.P.H., D.T.M.&H., Assistant County Medical Officer and District Medical Officer of Health for Wells Urban District Council and Docking and Walsingham Rural District Councils, Norfolk.

MOORHOUSE, DOREEN, M.B., Ch.B., Resident Medical Officer, the General Infirmary at Leeds.

NORTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD.—W. W. Brigden, M.D., F.R.C.P., Consultant Senior Cardiologist, Special Unit for Research into Juvenile Rheumatism, at Canadian Red Cross Memorial Hospital. Herta Graz, M.D., D.P.M., Consultant Child Psychiatrist at Portman Clinic. R. W. Rowan, M.D., M.R.C.P., Assistant Chest Physician, (S.H.M.O.), Edgware, Ealing and Harrow Chest Clinics. R. D. Young, M.B., Ch.B., M.R.C.P.Ed., Assistant Chest Physician (S.H.M.O.), Bedford Chest Clinic.

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—L. V. Martin, M.B., B.S., D.A., Consultant Anaesthetist in North Gloucestershire Clinical Area; S. Muscat, M.D., D.Obst.R.C.O.G., Registrar in Obstetrics and Gynaecology to Bath Group of Hospitals; D. R. Richard, B.M., B.Ch., Surgical Registrar at Weston-super-Mare General Hospital; E. J. Sanders, M.B., Ch.B., Surgical Registrar at Cheltenham General Hospital; C. D. R. Pengelly, M.B., Ch.B., M.R.C.P.Ed., Senior Medical Registrar to West Cornwall Clinical Area.

ZWIBFACH, E., M.D., F.R.C.S., D.L.O., Consultant Ear, Nose, and Throat Surgeon, West Middlesex Hospital.

BIRTHS, MARRIAGES, AND DEATHS

DEATHS

Ashby.—On December 1, 1953, at the Mercy Home, Cork, William Joseph Ashby, M.D., of Ashgates, Hettyfield Park, Cork, Eire.

Burt.—On December 1, 1953, at Pinderfields Hospital, Wakefield, Hutchison Burt, M.B., Ch.B., D.P.M., of Greenbank, Bar Lane, Wakefield, Yorks, aged 49.

Campbell.—On December 8, 1953, at the Windmill House, Ramsey, Essex, Samuel Marcus Dill Campbell, M.B., Ch.B., aged 77.

Cochrane.—On December 7, 1953, at home, Pinner, Middlesex, Thomas Cochrane, M.B., C.M., late of Peking, China, aged 87.

Greenwood.—On December 1, 1953, at his home, Birch House, Droylsden Road, Newton Heath, Manchester, Archer Greenwood, M.B., Ch.B.

Schofield.—On December 1, 1953, at Vine Cottage, Guildford, Surrey, Arthur Reginald Schofield, M.B., Surgeon Rear-Admiral, R.N., retired.

Sutton.—On November 27, 1953, at The Old Cottage, Long Melford, Suffolk, William Henry Arthur Douglas Sutton, O.B.E., L.R.C.P.&S.Ed., L.R.F.P.S., Colonel, late R.A.M.C., retired, aged 63.

Walker.—On November 29, 1953, Arthur Samuel Walker, M.D., D.P.H., of Middlesbrough, Yorks.

Warnock.—On December 4, 1953, in a nursing-home, Oxford, James Warnock, O.B.E., M.D., of Pull Croft, Sutton Courtenay, Berks, formerly of Chapel Allerton, Leeds, Yorks, aged 74.

Williams.—On November 27, 1953, in a nursing-home, Kirkby Lonsdale, Westmorland, Richard Geoffrey Williams, M.R.C.S., L.R.C.P., J.P., of Burrow, Carnforth, Lancs, aged 77.

Wilson.—On December 1, 1953, at Moorcroft, West Moors, Dorset, Arthur Harold Wilson, L.R.C.P.&S.Ed., L.R.F.P.S., D.P.H., formerly of East Wilts, aged 78.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Telling about Adoption

Q.—*What is the right age to tell a child that he has been adopted? How should it be done? How should the matter be broached if the telling has been delayed, for instance until the child is 10 or 12 years old?*

A.—The essential requirement is that at no time in the life of the child should there have been concealment of the fact of his adoption, or any untruth told about it. If this is observed, he will have become aware of the fact, without any surprise or shock, at the earliest age when the information would have any meaning for him. At some time he will have asked whether Aunt Jane is Mother's sister, or have made some similar inquiry, when, as part of an explanation that Aunt Jane is a courtesy aunt, he can be told of his adoption. In the same way, when questions are asked about how children are born, he could be told that Mother and the mother who bore him are different persons.

If the child has reached the age of 10 or 12 without being told, then the sooner he is told the better, with the minimum of fuss, though some formality will now scarcely be avoidable. A frank confession, with the statement that it was thought best to keep the truth from him till now, seems called for.

Persistent Laryngitis and Tracheitis

Q.—*What is the best treatment for persistent laryngitis and tracheitis?*

A.—First of all it must be clearly established by mirror laryngoscopy that there is no growth or paralysis of the larynx to account for the symptoms. When these causes have been excluded it is advisable to inquire into the state of the upper and lower respiratory tracts, as acute or chronic disease in the sinuses or lungs can perpetuate laryngitis or tracheitis.

Though tobacco rarely by itself causes irritation or infection of the respiratory tract, it can and does aggravate any inflammation of the mucosa lining the respiratory tract. Therefore, in any stubborn case of laryngitis and tracheitis it will be necessary to abandon tobacco. Avoidance of dusty, smoke-laden, or stuffy and over-heated atmospheres is also advisable. Local treatment can include any simple antiseptic throat lozenges in which may be incorporated a local analgesic such as benzocaine. The troublesome night cough can often be allayed by a hot drink, and inhalation of steam with Friar's balsam just before retiring may prevent it. In more stubborn cases a course of inhalations with a vaporizing attachment on an oxygen cylinder may be tried.

Inverted Nipples

Q.—*What is the best treatment for inverted nipples? Is the local inunction of oestrogen ointment effective?*

A.—Oestrogen ointment tends to develop the nipple and to make it more supple, and might help in the treatment of inverted nipples. In addition, however, during the second half of pregnancy some mechanical treatment is necessary, and this may take the form of daily digital manipulation or of periodic suction by an electric pump. One of the best lines of treatment, with or without the above measures, is to instruct the patient to wear "Waller"-type glass or plastic nipple-shields regularly.

Facial Disfigurement after Dental Extractions

Q.—*What measures can be taken to avoid the development of the disfiguring vertical grooves in the skin of the lips which appear a few years after dental extractions? They are particularly noticeable in middle-aged women and usually get progressively worse. Cannot dentures be built to avoid this, or will wearing them at night help? Alternatively, can established furrows be removed either by surgery or other means?*

A.—A deepening of the naso-labial fold invariably follows the extraction of all the teeth, the loss of the upper canines being the main cause. The effect can be minimized by the construction and wearing of "immediate dentures" and the continuous use of well-fitting plates: rarely can a denture be worn for more than a few years without requiring some alteration if the soft tissues are to remain fully supported. The dentures should be worn continuously, only being removed for cleaning.

Established furrows cannot be eliminated by prosthetic means, though much can be done to minimize them by judicious plumping of well-fitting dentures. For complete removal a plastic surgeon should be consulted.

Rectal Ether for Asthma

Q.—*Can you give me full instructions on the administration of rectal ether in oil for asthma? When is it indicated?*

A.—The usual dose is 5 to 7 oz. (140 to 200 ml.) of equal parts of olive oil and ether, depending on the weight of the patient (½ to 2 oz.—14 to 57 ml.—in children). The olive oil and ether must be thoroughly mixed, and are given slowly over about 20 minutes. Some authorities advise a cleansing enema first; others do not.

It is indicated, or rather was indicated, in status asthmaticus after adrenaline had failed. Introduced in 1931 and advocated as a life-saving measure, it came into very general and widespread use, but since the introduction of intravenous aminophylline in status asthmaticus the use of rectal ether and olive oil has declined to such an extent that it is now rarely used. At one time widely advocated in the literature, it is now seldom even referred to.

Rations for an Endurance Test

Q.—*What rations would be most suitable for a fit man undergoing a 25-hour endurance test in a canoe? The rations must be as light as possible, since they must be carried in the canoe during the test.*

A.—There may be good reason for a plentiful supply of protein to build up muscle and to replace wear and tear during training, but there should be no attempt to supply the energy for an endurance test from the body's proteins. Carbohydrate and fat are the most suitable sources of energy, and, since the metabolic cost of fat is thought to be greater, the ration for the test should consist mainly of carbohydrate. How much is required? If the athlete could maintain an oxygen consumption of one litre of oxygen a minute throughout the 25-hour test, his total energy expenditure would be 7,500 calories; this could be provided by approximately 1,300 g. of carbohydrate, with about 400 g. of fat and 200 g. of protein in addition. In simple terms, the energy requirements would be met approximately by a diet of 1½ lb. (0.68 kg.) of glucose and 1½ lb. of bread made up into sandwiches with butter and a ham or cheese filling. This spartan regime could be partly replaced by more attractive substitutes, according to the whim of the athlete, provided the proportions of the three basic foods were maintained. As much as possible of the carbohydrate should be taken in the form of sugar, and common sense will suggest that such slowly absorbed forms as potatoes should be avoided. It may be useful to make up the glucose with fruit juice. Several pints of this fluid may be taken during the test, and will help to make up the fluid and salt loss of the body, increase the alkaline reserve, and provide an immediate source of energy. A minimum requirement of fluid would be about 4 pints (2.3 litres), but thirst is as valuable a guide to water requirement as any other. It might be worth in addition taking two 5-gr. (0.32 g.) salt tablets at 8 and 16 hours, although the fruit juice would probably contain enough.

Selenium for Baldness

Q.—*Is selenium sulphide of value in the treatment of alopecia? If so, what are the indications for its use?*

A.—Selenium sulphide in the form of "selsun lotion" certainly appears to be useful in the control of dandruff of the scalp. However, although dandruff is often followed or accompanied by baldness (calvities) it cannot be assumed that the baldness has been caused by dandruff or that the suppression of dandruff will prevent the development of baldness.

While, therefore, this treatment has hardly been in use for a sufficient length of time to enable a judgment to be made, it seems unlikely that it can be expected to influence baldness.

NOTES AND COMMENTS

Pendulous Breasts.—Sir ARCHIBALD MCINDOE (London, W.1) writes: The rather old-womanish answer to the question on pendulous breasts ("Any Questions?" November 28, p. 1230) suggests that either they should be properly supported or the patient should go in for breast-stroke swimming, which is precisely what a woman would not want, and is almost invariably the reason why she seeks relief from the condition. Of course, the answer should have been that a surgical breast reduction should be performed by a competent plastic surgeon. This is an everyday operation and gives excellent results.

OUR EXPERT writes: This question and answer concerned the treatment of pendulous breasts *immediately* after cessation of breast-feeding, at which time there is much to be said for conservative measures—particularly if the patient is young and likely to have more children. Sir Archibald McIndoe's comment applies more to the treatment of breasts which remain pendulous after involution is complete and which are unlikely to be exposed again to the stimulus of pregnancy and lactation.

Causes of Failure of Contraceptive Diaphragms.—Dr. LILIAS M. JEFFRIES (Hove) writes: Referring to the question about the causes of failure to prevent conception by the use of the Dutch cap ("Any Questions?" November 28, p. 1229), I have found that a common cause is constipation. Scybala distort the shape of the vagina. Patients are often unconscious that the rectum is loaded, and need to be warned that the cap has been fitted when the bowel is empty, so that it will not fit otherwise. It is well worth while drawing attention to this point.

"Any Questions?" Book.—The second book of selected "Any Questions?" is available, price 7s. 6d. (postage 6d.). Copies may be obtained either direct from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or from booksellers.

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